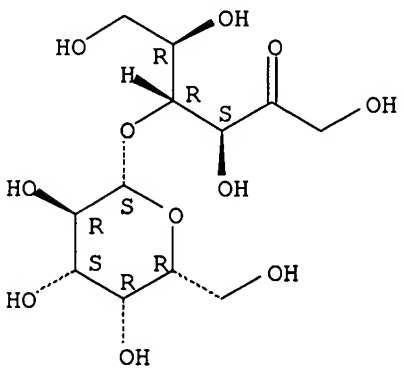
8/16

L1 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 4618-18-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Fructose, 4-O-β-D-galactopyranosyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Fructose, 4-O-β-D-galactopyranosyl-, D- (8CI)
CN Lactulose (6CI, 7CI)
OTHER NAMES:
CN 4-O-β-D-Galactopyranosyl-D-fructose
CN Bifiteral
CN Cephulac
CN D-Lactulose
CN Duphalac
CN Farlac
CN Generlac
CN Isolactose
CN Lactuflor
CN Laevilac
CN Laevolac
CN Laktusan
CN Lazet
CN Milk Oligosaccharide MLP 95
CN MLC 97
CN MLS 50
CN Normase
CN Well-me
FS STEREOSEARCH
DR 576-08-9, 29319-45-7, 33980-82-4, 40773-84-0
MF C12 H22 O11
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, PS, RTECS*, SCISEARCH, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

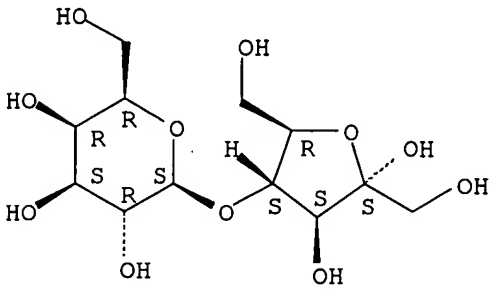
1515 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1526 REFERENCES IN FILE CAPLUS (1907 TO DATE)

33 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d 10-12

L1 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 58166-25-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN α-D-Fructofuranose, 4-O-β-D-galactopyranosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN α-Lactulose
FS STEREOSEARCH
MF C12 H22 O11
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, CSCHEM, SPECINFO, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

National Library of Medicine - Medical Subject Headings

2006 MeSH

MeSH Descriptor Data

Return to Entry Page

MeSH Heading	Hepatic Encephalopathy
Tree Number	C06.552.308.500.356
Tree Number	C10.228.140.163.360
Tree Number	C18.452.100.360
Scope Note	A syndrome characterized by central nervous system dysfunction in association with LIVER FAILURE, including portal-systemic shunts. Clinical features include lethargy and CONFUSION (frequently progressing to COMA); ASTERIXIS; NYSTAGMUS, PATHOLOGIC; brisk oculovestibular reflexes; decorticate and decerebrate posturing; MUSCLE SPASTICITY; and bilateral extensor plantar reflexes (see REFLEX, BABINSKI). ELECTROENCEPHALOGRAPHY may demonstrate triphasic waves. (From Adams et al., Principles of Neurology, 6th ed, pp1117-20; Plum & Posner, Diagnosis of Stupor and Coma, 3rd ed, p222-5)
Entry Term	Encephalopathy, Hepatic
Entry Term	Portosystemic Encephalopathy
Entry Term	Encephalopathy, Hepatocerebral
Entry Term	Encephalopathy, Portal-Systemic
Entry Term	Encephalopathy, Portosystemic
Entry Term	Fulminant Hepatic Failure with Cerebral Edema
Entry Term	Hepatic Coma
Entry Term	Hepatic Stupor
Entry Term	Hepatocerebral Encephalopathy
Entry Term	Portal-Systemic Encephalopathy
Allowable Qualifiers	BL CF CI CL CN CO DH DI DT EC EH EM EN EP ET GE HI IM ME MI MO NU PA PC PP PS PX RA RH RI RT SU TH UR US VE VI
Entry Version	HEPATIC ENCEPH

History Note	1984; use HEPATIC COMA 1975-83
Unique ID	D006501

MeSH Tree Structures

Digestive System Diseases [C06]
- Liver Diseases [C06.552]
  - Hepatic Insufficiency [C06.552.308]
    - Liver Failure [C06.552.308.500]
      - ▶ Hepatic Encephalopathy [C06.552.308.500.356]
      - Liver Failure, Acute [C06.552.308.500.750] +

Nervous System Diseases [C10]
- Central Nervous System Diseases [C10.228]
  - Brain Diseases [C10.228.140]
    - Brain Diseases, Metabolic [C10.228.140.163]
      - Brain Diseases, Metabolic, Inborn [C10.228.140.163.100] +
      - ▶ Hepatic Encephalopathy [C10.228.140.163.360]
      - Kernicterus [C10.228.140.163.480]
      - Mitochondrial Encephalomyopathies [C10.228.140.163.540]
      - Myelinolysis, Central Pontine [C10.228.140.163.560]
      - Reye Syndrome [C10.228.140.163.780]
      - Wernicke Encephalopathy [C10.228.140.163.960]

Nutritional and Metabolic Diseases [C18]
- Metabolic Diseases [C18.452]
  - Brain Diseases, Metabolic [C18.452.100]
    - Brain Diseases, Metabolic, Inborn [C18.452.100.100] +
    - ▶ Hepatic Encephalopathy [C18.452.100.360]
    - Kernicterus [C18.452.100.480]
    - Mitochondrial Encephalomyopathies [C18.452.100.540]
    - Myelinolysis, Central Pontine [C18.452.100.560]
    - Reye Syndrome [C18.452.100.780]
    - Wernicke Encephalopathy [C18.452.100.960]

Return to Entry Page **Link to NLM Cataloging Classification**

Connecting via Winsock to STN

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	4	APR 04	STN AnaVist $500 visualization usage credit offered
NEWS	5	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS	6	MAY 11	KOREAPAT updates resume
NEWS	7	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS	8	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS	9	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS	10	JUN 02	The first reclassification of IPC codes now complete in INPADOC
NEWS	11	JUN 26	TULSA/TULSA2 reloaded and enhanced with new search and and display fields
NEWS	12	JUN 28	Price changes in full-text patent databases EPFULL and PCTFULL
NEWS	13	JUl 11	CHEMSAFE reloaded and enhanced
NEWS	14	JUl 14	FSTA enhanced with Japanese patents
NEWS	15	JUl 19	Coverage of Research Disclosure reinstated in DWPI
NEWS	16	AUG 09	INSPEC enhanced with 1898-1968 archive

NEWS EXPRESS	JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 22:38:41 ON 16 AUG 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 22:39:02 ON 16 AUG 2006

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 15 AUG 2006 HIGHEST RN 901654-60-2
DICTIONARY FILE UPDATES: 15 AUG 2006 HIGHEST RN 901654-60-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

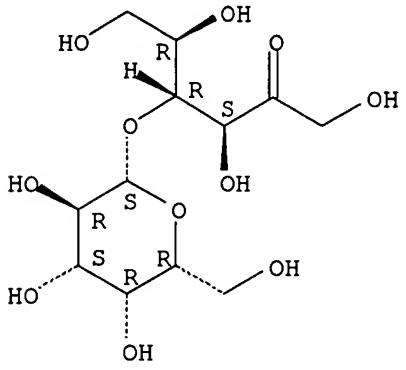
=> s lactulose
L1 13 LACTULOSE

=> d 13

L1 ANSWER 13 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 4618-18-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN D-Fructose, 4-O-β-D-galactopyranosyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Fructose, 4-O-β-D-galactopyranosyl-, D- (8CI)
CN Lactulose (6CI, 7CI)
OTHER NAMES:
CN 4-O-β-D-Galactopyranosyl-D-fructose
CN Bifiteral
CN Cephulac
CN D-Lactulose
CN Duphalac
CN Farlac
CN Generlac
CN Isolactose
CN Lactuflor
CN Laevilac
CN Laevolac
CN Laktusan
CN Lazet
CN Milk Oligosaccharide MLP 95
CN MLC 97
CN MLS 50
CN Normase
CN Well-me
FS STEREOSEARCH
DR 576-08-9, 29319-45-7, 33980-82-4, 40773-84-0
MF C12 H22 O11
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO,
CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN,
CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB,

IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, PS, RTECS*, SCISEARCH, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



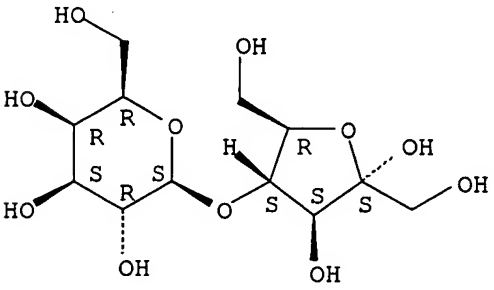
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1515 REFERENCES IN FILE CA (1907 TO DATE)
27 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1526 REFERENCES IN FILE CAPLUS (1907 TO DATE)
33 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d 10-12

L1 ANSWER 10 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 58166-25-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN α-D-Fructofuranose, 4-O-β-D-galactopyranosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN α-Lactulose
FS STEREOSEARCH
MF C12 H22 O11
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, CSCHEM, SPECINFO, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.

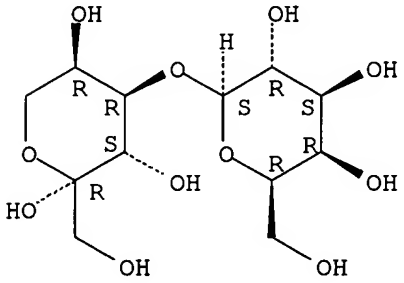


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 11 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 58166-23-7 REGISTRY
ED Entered STN: 16 Nov 1984
CN β-D-Fructopyranose, 4-O-β-D-galactopyranosyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN β-Lactulose
FS STEREOSEARCH
MF C12 H22 O11
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, SPECINFO
(*File contains numerically searchable property data)

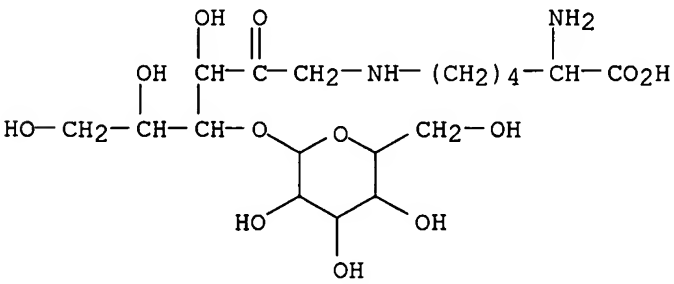
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 12 OF 13 REGISTRY COPYRIGHT 2006 ACS on STN
RN 34326-63-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Lysine, N6-(1-deoxy-4-O-β-D-galactopyranosyl-D-fructos-1-yl)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN D-Fructose, 1-[(5-amino-5-carboxypentyl)amino]-1-deoxy-4-O-β-D-galactopyranosyl-, (S)-
CN Fructose, 1-[(L-5-amino-5-carboxypentyl)amino]-1-deoxy-4-O-β-D-galactopyranosyl-, D- (8CI)
OTHER NAMES:
CN ε-Lactuloselysine
CN Lactuloselysine
MF C18 H34 N2 O12
LC STN Files: AGRICOLA, ANABSTR, BIOSIS, CA, CAPLUS, MEDLINE, TOXCENTER



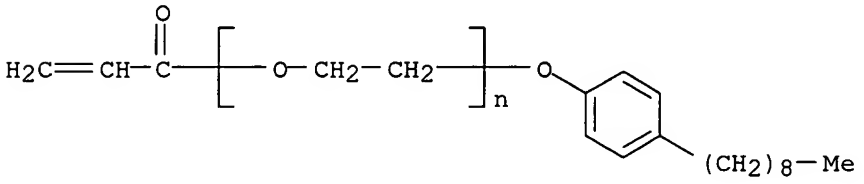
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

32 REFERENCES IN FILE CA (1907 TO DATE)
32 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s polyethylene glycol
8939 POLYETHYLENE
51392 GLYCOL
714 GLYCOLS
51392 GLYCOL
(GLYCOL OR GLYCOLS)
L2 7708 POLYETHYLENE GLYCOL
(POLYETHYLENE(W)GLYCOL)

=> d 7708

L2 ANSWER 7708 OF 7708 REGISTRY COPYRIGHT 2006 ACS on STN
RN 2073-54-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(1-oxo-2-propenyl)-ω-(4-nonylphenoxy)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Aronix M 113
CN Aronix M 114
CN Aronix X 511A
CN Aronix X 513A
CN Light Acrylate NP 10EA
CN M 113
CN M 114
CN Newfrontier 177E
CN NP 10EA
CN Polyethylene glycol mono(4-nonylphenyl) ether monoacrylate
CN Polyethylene glycol p-nonylphenyl ether acrylate
DR 161635-88-7, 105096-64-8, 113755-55-8, 136748-97-5, 82658-36-4, 81605-44-9, 92481-14-6
MF (C2 H4 O)n C18 H26 O2
CI PMS, COM
PCT Polyether
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER, USPAT2, USPATFULL



116 REFERENCES IN FILE CA (1907 TO DATE)
31 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
116 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s l2 and peg
303 PEG
2 PEGS
305 PEG

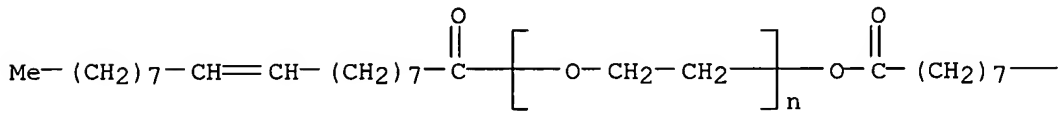
(PEG OR PEGS)
L3 69 L2 AND PEG

=> d 60-69

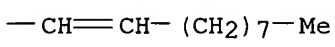
L3 ANSWER 60 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9005-07-6 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-[[(9Z)-1-oxo-9-octadecenyl]oxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, dioleate (8CI)
CN Oleic acid, diester with polyethylene glycol (8CI)
CN Poly(oxy-1,2-ethanediyl), α-(1-oxo-9-octadecenyl)-ω-[(1-oxo-9-octadecenyl)oxy]-, (Z,Z)-
OTHER NAMES:
CN α-Oleoyl-ω-(oleoyloxy)poly(oxyethylene)
CN Alkamuls 600DO
CN Alkasurf 400DO
CN Alkasurf 600DO
CN Atlas G 2242
CN Chromasist 188A
CN Chromassist 188A
CN Cithrol 4DO
CN DO 1000
CN Emalex 300di-O
CN Emalex 400di-O
CN Emalex 600di-O
CN Emerest 2648
CN Esterol 244
CN Esterol 263
CN Ethox DO 14
CN Ethox DO 9
CN G 2242
CN Ionet DO
CN Ionet DO 1000
CN Ionet DO 200
CN Ionet DO 400
CN Ionet DO 600
CN Kessco PEG 1540DO
CN Lipo-Peg 30
CN Lipopeg 4DO
CN Lumulse 62O
CN Mapeg 200DO
CN Mapeg 400DO
CN Mapeg 6000
CN Mapeg 600DO
CN Marlipal FS
CN Marlosol FS
CN Nonex 68
CN Nonex 69
CN PEG 200 dioleate
CN PEG 32 dioleate
CN PEG 400 dioleate
CN Pegnol O 24
CN Pegosperse 400DO
CN Pionin D 2506D
CN Polyethylene glycol dioleate
CN Polyethylene oxide dioleate
CN Polyoxyethylene dioleate
CN Radiasurf 7443
DR 9009-91-0, 57425-46-4
MF (C2 H4 O)n C36 H66 O3

CI PMS, COM
PCT Polyether
LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, CIN, CSCHEM, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, TOXCENTER, USPAT2, USPATFULL
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

PAGE 1-A



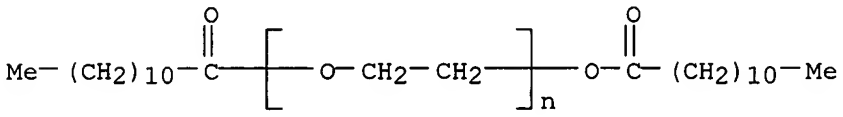
PAGE 1-B



362 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
363 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 61 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9005-02-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(1-oxododecyl)-ω-[(1-oxododecyl)oxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, dilaurate (8CI)
CN Lauric acid, diester with polyethylene glycol (8CI)
OTHER NAMES:
CN Cithrol 4DL
CN Coadjuvant Chevron
CN Emerest 2622
CN Emerest 2652
CN Ethox DL 14
CN Ethox DL 5
CN Ethox DL 9
CN Hodag 22L
CN Ionet DL 1000
CN Ionet DL 200
CN Jeemate 400DL
CN Jeemate 600DL
CN Kessco PEG 1540DL
CN Kessco PEG 200DL
CN Kessco PEG 300DL
CN Kessco PEG 600DL
CN Lipopeg 4DL
CN Mapeg 200DL
CN Mapeg 400DL
CN Nonex 104
CN PEG 600 dilaurate
CN PEG 8 Dilaurate
CN PEG dilaurate
CN Pegosperse 200DL
CN Pegosperse 400DL
CN Polyethylene glycol didodecanoate
CN Polyethylene glycol dilaurate

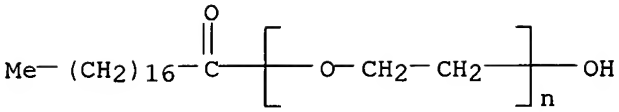
CN Polyethylene oxide didodecanoate
CN Polyethylene oxide dilaurate
CN Polyoxyethylene dilaurate
CN Suspensif 2643
CN Uniplex 810
MF (C2 H4 O)n C24 H46 O3
CI PMS
PCT Polyether
LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



305 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
307 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 62 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-99-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(1-oxooctadecyl)-ω-hydroxy- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Stearic acid, monoester with polyethylene glycol (8CI)
OTHER NAMES:
CN 40S
CN 40S (polyether)
CN 60S
CN 60S (polyether)
CN Akyporox S 100
CN Alkasurf S 65-8
CN Arosurf 1855E40
CN Atlox 5000
CN Capcure 65
CN Carbowax 1000 monostearate
CN Carbowax 1500 monostearate
CN Carbowax 4000 monostearate
CN Cerasynt 660
CN Cerasynt 840
CN Cerasynt M
CN Cerasynt MN
CN Chemax E 1750MS
CN Chemax E 400MS
CN Cithrol 10MS
CN Cithrol 4MS
CN Cithrol PS
CN Clearate G
CN Cremofor 410R
CN Cremophor 410R
CN Cremophor S 9
CN Crill 20
CN Crill 21
CN Crill 22
CN Crill 23
CN Crodet S

CN Crodet S 100
CN Crodet S 24
CN E 430
CN Emalex 6300M-ST
CN Emalex 804
CN Emanon 3113
CN Emanon 3115
CN Emanon 3119
CN Emanon 3170
CN Emanon 3199
CN Emcol H 35A
CN Emerest 2640
CN Emerest 2662
CN Emerest 2715
CN Emery 15393
CN Empilan CP 100
CN Empilan CQ 100
CN Ethofat 60/15
CN Ethofat 60/20
CN Ethofat 60/25
CN Kessco PEG 1540MS
CN Kessco PEG 6000MS
CN PEG 1000 monostearate
CN PEG 1000MS
CN PEG 100MS
CN PEG 150 Stearate
CN PEG 40 Stearate
CN PEG 42
CN PEG 600 monostearate
CN PEG 600MS
CN PEG 8 Stearate
CN PEG stearate
CN PEG-40M
CN Polyethylene glycol 100 monostearate
CN Polyethylene glycol 1540 stearate
CN Polyethylene glycol 200 monostearate
CN Polyethylene glycol 300 monostearate
CN Polyethylene glycol 3000 monostearate
CN Polyethylene glycol 40 monostearate
CN Polyethylene glycol 400 monostearate
CN Polyethylene glycol 400 stearate
CN Polyethylene glycol 4000 monostearate
CN Polyethylene glycol monostearate
CN Polyethylene glycol monostearic acid ester
CN Polyethylene glycol stearate
CN Tegester PEG
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 8035-96-9, 8050-55-3, 9009-90-9, 11107-94-1, 11108-48-8, 53228-13-0, 53335-42-5, 58375-39-6, 123543-87-3, 121340-91-8, 63654-37-5, 35885-17-7, 72993-78-3, 74870-86-3, 86473-52-1, 39404-30-3, 42610-76-4, 52504-21-9, 52504-22-0, 52504-23-1
MF (C2 H4 O)n C18 H36 O2
CI PMS, COM
PCT Polyether
LC STN Files: AQUIRE, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

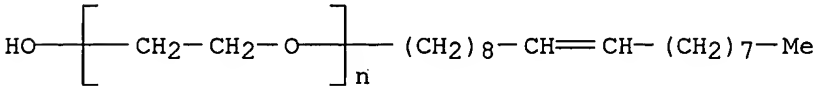


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3586 REFERENCES IN FILE CA (1907 TO DATE)
71 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3602 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 63 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-98-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(9Z)-9-octadecenyl-ω-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9-Octadecen-1-ol, monoether with polyethylene glycol, (Z)- (8CI)
OTHER NAMES:
CN 9-Octadecen-1-ol-ethylene oxide copolymer
CN Ahco 3998
CN Ameroxol OE 10
CN Ameroxol OE 2
CN Ameroxol OE 20
CN Atlas G 3915
CN Atlas G 3920
CN Atmer 137
CN Blaunon EN 1504
CN Blaunon EN 1530
CN Blaunon EN 1540
CN Blaunon EN 905
CN Blaunon EN 909
CN BO 15TX
CN BO 15V
CN BO 2
CN BO 20
CN BO 20V
CN BO 7
CN Brij 92
CN Brij 93
CN Brij 93Veg
CN Brij 96
CN Brij 96v
CN Brij 97
CN Brij 98
CN Brij 98V
CN Brij 99
CN Chemal OA 9
CN E 205S
CN E 212
CN Emalex 503
CN Emalex 505
CN Emalex 505H
CN Emalex 506
CN Emalex 510
CN Emalex 515
CN Emalex 515H
CN Emalex 520
CN Emalex 550
CN Emalex 550P

CN Emulgen 3200
CN Emulgen 404
CN Emulgen 408
CN Emulgen 409P
CN Emulgen 420
CN Emulgen 430
CN Emulgen 490P
CN Emulphor O
CN Oleyl alcohol polyethyleneglycol ether
CN PEG-20 oleyl ether
CN Polyethylene glycol mono-9-octadecenyl ether
CN Polyethylene glycol monooleyl ether
CN Polyethylene glycol oleyl ether
CN Polyethyleneglycol monooctadecenyl ether
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 37702-39-9
DR 726175-59-3, 170516-63-9, 8013-81-8, 8036-15-5, 8036-16-6, 9007-63-0, 158453-78-2, 159131-59-6, 126879-46-7, 54351-97-2, 58056-96-5, 58857-52-6, 50957-68-1, 51888-74-5, 115453-13-9, 61276-84-4, 65431-57-4, 37230-81-2, 37260-66-5, 37317-52-5, 37332-04-0, 37332-05-1, 37336-10-0, 37336-11-1, 37370-70-0, 145613-04-3, 79586-81-5, 80701-83-3, 31586-45-5, 31899-57-7, 32054-74-3, 32236-19-4, 39384-39-9, 52440-04-7, 52452-85-4, 52627-03-9, 53124-83-7, 191549-76-5, 647858-18-2
MF (C2 H4 O)n C18 H36 O
CI PMS, COM
PCT Polyether
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



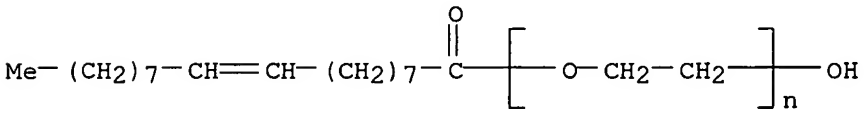
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3660 REFERENCES IN FILE CA (1907 TO DATE)
92 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3662 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 64 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-96-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-[(9Z)-1-oxo-9-octadecenyl]-ω-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Oleic acid, monoester with polyethylene glycol (8CI)
OTHER NAMES:
CN Adeka Estol OEG 204
CN Akyporox O 50
CN Alkamuls 400MO
CN Alkasurf O 14
CN Alkasurf O 75-9
CN Atlas G 2142
CN Atlas G 2143

CN Atlas G 2144
CN Atlas G 5507
CN Atlas G 5511
CN Blaunon O 600SA
CN Cemulsol 1050
CN Cemulsol A
CN Cemulsol C 105
CN Cemulsol D 8
CN Chemax E 400MO
CN Chemester 300OC
CN Cithrol 2MO
CN Cithrol PO
CN CRL 1337
CN Crodet O 100
CN Crodet O 40
CN Crodet O 6
CN Dyapol G
CN E2
CN Emalex 218
CN Emalex OE 1
CN Emalex OE 10
CN Emanon 4110
CN Emanon 4115
CN Emcol H 2A
CN Emcol H 31A
CN Emerest 2624
CN Emerest 2646
CN Emerest 2660
CN Empilan BP 100
CN Empilan BQ 100
CN Emulan A
CN Emulphor 24
CN Emulphor A
CN Emulphor VN 430
CN EN 1507
CN EN 1511
CN ES 120
CN Estax 38 S.F
CN Estax 38SE
CN Ethofat O
CN Ethofat O 15
CN Ethofat O 20
CN Ethox MO 14
CN Kessco PEG 1000MO
CN Kessco PEG 400MO
CN Lipo-Peg 4O
CN Monooleate ester of polyethylene glycol
CN PEG 1000MO
CN PEG 200MO
CN PEG 300 monooleate
CN PEG 400MO
CN PEG 600MO
CN PEG-20 Oleate
CN PEG-32 Oleate
CN PEG-400 oleate
CN PEG-6 Oleate
CN Polyethylene glycol monooleate
CN Polyethylene glycol oleate
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 12789-13-8, 8013-78-3, 8051-25-0, 9007-68-5, 1341-62-4, 55126-82-4, 55945-62-5, 103939-39-5, 37223-98-6, 37223-99-7, 37330-99-7, 67775-15-9, 141927-22-2, 82905-19-9, 39316-40-0, 41139-27-9, 52504-20-8

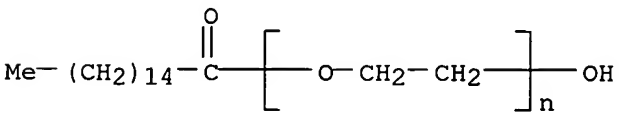
MF (C2 H4 O)n C18 H34 O2
CI PMS, COM
PCT Polyether
LC STN Files: ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1495 REFERENCES IN FILE CA (1907 TO DATE)
35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1496 REFERENCES IN FILE CAPLUS (1907 TO DATE)

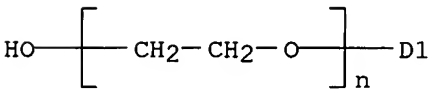
L3 ANSWER 65 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-94-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(1-oxohexadecyl)-ω-hydroxy- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, monopalmitate (8CI)
CN Palmitic acid, monoester with polyethylene glycol (8CI)
OTHER NAMES:
CN Atlas G 2076
CN Atlas G 2079
CN G 2079
CN Nissan Nonion P 6
CN Nonion P 6
CN PEG-6 Palmitate
CN Poly(oxyethylene) monopalmitate
CN Polyethylene glycol ester of palmitic acid
CN Polyethylene glycol monopalmitate
CN Polyethylene glycol palmitate
CN Polyethylene glycol palmitate ester
CN Polynon P 101
CN Polyoxyethylene glycol monopalmitate
CN Polyoxyethylene palmitate
CN Polyoxyethylene-30 palmitate
DR 53228-20-9, 53251-37-9, 63849-66-1
MF (C2 H4 O)n C16 H32 O2
CI PMS, COM
PCT Polyether
LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, CHEMLIST, CSCHEM, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPAT2, USPATFULL
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



186 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
187 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 66 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-87-9 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(isooctylphenyl)-ω-hydroxy- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, mono(isooctylphenyl) ether (8CI)
CN Phenol, isooctyl-, monoether with polyethylene glycol (8CI)
OTHER NAMES:
CN (Isooctylphenoxy)poly(ethylene oxide)
CN (Isooctylphenoxy)poly(oxyethylene)ethanol
CN (Isooctylphenoxy)polyethoxyethanol
CN (Isooctylphenyl)polyethylene oxide
CN Ethoxylated isooctylphenol
CN Ethylene oxide-isooctylphenol adduct
CN Isooctylphenolpolyethoxyethanol
CN Isooctylphenyl polyethoxyethanol
CN OP 12.8
CN OP 7
CN OP 8.9
CN PEG isooctylphenyl ether
CN Phenoxol
CN Polyethoxylated isooctylphenol
CN Polyethylene glycol isooctylphenyl ether
CN Polyethylene glycol mono(isooctylphenyl) ether
CN Polyoxyethylene isooctylphenyl ether
CN Romopal OF 10
CN SV 105-12
CN Triton 11XE
CN Triton X 1000
DR 11099-59-5, 76037-22-4
MF (C2 H4 O)n C14 H22 O
CI IDS, PMS, COM
PCT Polyether
LC STN Files: BIOSIS, CA, CAPLUS, CASREACT, CHEMLIST, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

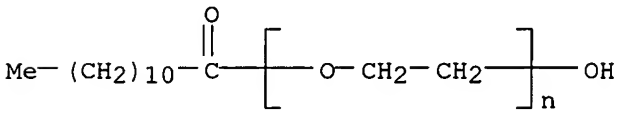
D1— (C_8H_{17})



437 REFERENCES IN FILE CA (1907 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
438 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 67 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-81-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-(1-oxododecyl)-ω-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, monolaurate (8CI)
CN Lauric acid, monoester with polyethylene glycol (8CI)
OTHER NAMES:
CN α-Lauroyl-ω-hydroxypoly(oxyethylene)
CN Aquafil I
CN Aquafil II
CN Atlas G 2109
CN Atlas G 2127
CN Atlas G 2129
CN Blaunon L 400
CN Brian L
CN Brian L 400
CN Cirrasol TCS
CN Cithrol 2ML
CN Cithrol 6ML
CN CPH 376N
CN Crodet L
CN Crodet L 100
CN Crodet L 12
CN Crodet L 24
CN Crodet L 4
CN Crodet L 40
CN Crodet L 8
CN Deplastol
CN Emanon 1112
CN Emanon 1112HG
CN Emerest 2620
CN Emerest 2650
CN Empilan AP 100
CN Empilan AQ 100
CN Ethox ML 14
CN Ethox ML 5
CN Ethox ML 9
CN Ethylan L
CN Ethylan L 3
CN G 2127
CN G 2129
CN Hallco CPH 43
CN Ionet ML 400
CN Jeemate 400ML
CN Kessco PEG 1000ML
CN Kessco PEG 400ML
CN Kessco PEG 600
CN Kessco PEG 600ML
CN Laurox 9
CN Lipo-Peg 4L
CN Lonzest PEG 4L
CN Lumulse 40L
CN Macrogol laurate 600
CN Mapeg 200ML
CN Mapeg 400ML
CN PEG 200 monolaurate
CN Polyethylene glycol dodecyl ester
CN Polyethylene glycol laurate
CN Polyethylene glycol lauric acid ester
CN Polyethylene glycol lauryl ester
CN Polyethylene glycol monolaurate

CN Polyethylene glycol monolauryl ester
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 8050-58-6, 9009-89-6, 53228-21-0, 53251-33-5, 53663-49-3, 58392-04-4, 57608-70-5, 102685-35-8, 36509-57-6, 37273-92-0, 37334-88-6, 37336-48-4, 150419-02-6, 86727-30-2
MF (C2 H4 O)n C12 H24 O2
CI PMS, COM
PCT Polyether
LC STN Files: AGRICOLA, AQUIRE, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, MEDLINE, MSDS-OHS, PIRA, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

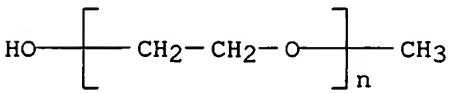


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1219 REFERENCES IN FILE CA (1907 TO DATE)
39 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1221 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 68 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9004-74-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-methyl-ω-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycols, polyethylene, monomethyl ether (8CI)
OTHER NAMES:
CN α-Methyl-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN 2,5,8,11,14,17,20,23,26,29,32,35,38,41,44,47,50-Heptadecaoxadopentacontan-52-ol
CN Breox MPEG 550
CN Carbowax 2000
CN Carbowax 350
CN Carbowax 5000
CN Carbowax 550
CN Carbowax 750
CN Carbowax 750ME
CN Carbowax MPEG 450
CN Carbowax MPEG 5000
CN Conion MP 220
CN CP 2000
CN CP 2000 (polyoxyalkylene)
CN Ethylene oxide-methanol adduct
CN GN 8384
CN Hymol PM
CN M 550
CN M 750
CN Marlipal 1/12
CN Me-PEG 400
CN Methoxy PEG 400
CN Methoxypoly(ethylene glycol)
CN Methyl polyglycol

CN Monomethoxy poly(ethylene oxide)
CN Monomethoxypolyethylene glycol
CN Monomethoxypolyoxyethylene
CN MPEG
CN MPEG 10000
CN MPEG 2000
CN MPEG 350
CN MPEG 500
CN MPEG 5000
CN MPEG 550
CN MPEG 750
CN MPEG 950
CN MPG
CN MPG 025
CN MPG 081
CN MPG 130
CN MPG 130H
CN MPG 140
CN Nissan Uniol 1000
CN Nissan Uniol 550
CN Nissan Uniox M 1000
CN Nissan Uniox M 2000
CN Nissan Uniox M 400
CN Nissan Uniox M 4000
CN Nissan Uniox M 550
CN O-Methoxypolyethylene glycol
CN PEG-MME
CN Polyethylene glycol methyl ether
CN Polyethylene glycol monoether with methyl diglycol
CN Polyethylene glycol monomethyl ether
CN Toho Me-PEG 1000
CN Toho Me-PEG 400
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 251911-64-5
DR 165338-17-0, 12623-96-0, 163294-10-8, 163733-28-6, 162582-19-6, 166441-82-3, 158360-78-2, 126966-17-4, 54386-07-1, 57244-93-6, 64543-87-9, 134919-42-9, 95507-78-1, 95507-80-5, 102868-77-9, 104841-59-0, 138753-86-3, 69592-91-2, 72664-19-8, 77102-87-5, 142172-77-8, 146162-92-7, 154701-70-9, 154885-26-4, 86002-19-9, 91826-72-1, 41396-14-9, 178613-33-7, 185250-24-2, 187523-66-6, 189209-93-6, 193008-24-1, 195970-98-0, 207799-14-2, 212969-32-9, 216693-45-7, 226212-72-2, 237739-71-8, 241466-57-9, 396134-26-2, 438245-23-9
MF (C2 H4 O)n C H4 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DETHERM*, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

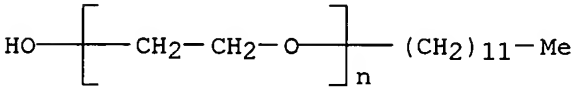


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3837 REFERENCES IN FILE CA (1907 TO DATE)
1408 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3845 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 69 OF 69 REGISTRY COPYRIGHT 2006 ACS on STN
RN 9002-92-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN Poly(oxy-1,2-ethanediyl), α-dodecyl-ω-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dodecyl alcohol, monoether with polyethylene glycol (8CI)
OTHER NAMES:
CN α-Dodecyl-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN α-Dodecyl-ω-hydroxypoly(oxyethylene)
CN 40L
CN 40L (polyether)
CN Actinol L 3
CN Actinol L 7
CN Adeka Carpol MBF 100
CN Adekatol LA 1275
CN Adekatol LA 50
CN Aethoxysklerol
CN Aetoxisclerol
CN Agrimul NRE-C12 EO5
CN Akyporox RLM 160
CN Akyporox RLM 22
CN Akyporox RLM 230
CN Akyporox RLM 40
CN Aldosperse L 9
CN Alkasurf LAN 1
CN Alkasurf LAN 3
CN Arapol 0712
CN Arylpon F
CN Atlas G 2133
CN Atlas G 3705
CN Atlas G 3707
CN Atlas G 4829
CN Atmer 135
CN B 205
CN Base LP 12
CN BL 2
CN BL 9
CN BL 9 (polyglycol)
CN BL 9EX
CN Blaunon EL 1503P
CN Blaunon EL 1509
CN Brij 22
CN Brij 23
CN Brij 30
CN Brij 30ICI
CN Brij 30SP
CN Brij 35
CN Brij 35L
CN Brij 35P
CN Brij 35P Nena
CN Brij 36T
CN Calgene 40L
CN Carsonol L 2
CN Carsonol L 3
CN Chemal LA 23
CN Chemal LA 4
CN Chimipal AE 3
CN Lauryl polyethylene glycol ether

CN PEG dodecyl ether
CN PEG n-dodecyl ether
CN Polyethylene glycol dodecyl ether
CN Polyethylene glycol dodecyl monoether
CN Polyethylene glycol lauryl alcohol ether
CN Polyethylene glycol lauryl ether
CN Polyethylene glycol monododecyl ether
CN Polyethylene glycol monolauryl ether
CN Polyethylene glycol n-dodecyl ether
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 798544-27-1, 869893-21-0, 503027-85-8, 504414-58-8, 6540-99-4, 8027-11-0, 9015-55-8, 9079-21-4, 11106-34-6, 1334-72-1, 1341-05-5, 122779-58-2, 53241-34-2, 54351-54-1, 54398-17-3, 56590-57-9, 56939-70-9, 57244-90-3, 124401-71-4, 55599-84-3, 55892-94-9, 56093-86-8, 64772-19-6, 62229-27-0, 101840-74-8, 102329-60-2, 102342-03-0, 106254-08-4, 106254-09-5, 50815-85-5, 50815-86-6, 51426-13-2, 61373-94-2, 61710-38-1, 37231-23-5, 37343-87-6, 137736-73-3, 138100-08-0, 69344-85-0, 71932-08-6, 71636-71-0, 141875-75-4, 147398-17-2, 148093-10-1, 152206-24-1, 86547-02-6, 86727-31-3, 87296-34-2, 31798-98-8, 39316-02-4, 39316-41-1, 39363-77-4, 53026-66-7, 101008-55-3, 106856-65-9, 176235-62-4, 176596-95-5, 183117-57-9, 186762-97-0, 189388-50-9, 191546-41-5, 201746-17-0, 221642-91-7, 234761-81-0, 234761-82-1, 234761-83-2, 234764-37-5, 266678-04-0, 348616-52-4, 359786-16-6, 362661-71-0, 384842-79-9, 459409-03-1
MF (C2 H4 O)n C12 H26 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, PROMT, RTECS*, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10115 REFERENCES IN FILE CA (1907 TO DATE)
247 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10139 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	49.30	49.51

FILE 'MEDLINE' ENTERED AT 22:41:19 ON 16 AUG 2006

FILE LAST UPDATED: 16 Aug 2006 (20060816/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details

```
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> file caplus medline biosis embase
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               1.56      51.07

FILE 'CAPLUS' ENTERED AT 22:43:26 ON 16 AUG 2006
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=> s 4618-18-2/rn or lactulose or cephulac or 576-08-9/rn or 29319-45-7/rn or
33980-82-4/rn or 40773-84-0/rn
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
'RN' IS NOT A VALID FIELD CODE
L4         9940 4618-18-2/RN OR LACTULOSE OR CEPHULAC OR 576-08-9/RN OR 29319-45
                -7/RN OR 33980-82-4/RN OR 40773-84-0/RN

=> s l4 and (peg or polyethylene glycol)
L5          231 L4 AND (PEG OR POLYETHYLENE GLYCOL)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6          129 DUP REM L5 (102 DUPLICATES REMOVED)

=> focus
PROCESSING COMPLETED FOR L6
L7          129 FOCUS L6 1-

=> s l7 and (combo? or combi? or together or coadmini? or co-admin? or concurrent?
or same time or mix?)
L8           25 L7 AND (COMBO? OR COMBI? OR TOGETHER OR COADMINI? OR CO-ADMIN?
                OR CONCURRENT? OR SAME TIME OR MIX?)

=> focus
PROCESSING COMPLETED FOR L8
L9           25 FOCUS L8 1-

=> d ibib abs 1-25
```

L9 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:32896 CAPLUS
DOCUMENT NUMBER: 124:140314
TITLE: Effect of water-loading on the performance of polyethylene glycol as a marker of small intestinal permeability
AUTHOR(S): Iqbal, Tariq H.; Cox, Mark A.; Lewis, Kenneth O.; Cooper, Brian T.
CORPORATE SOURCE: Gastroenterology Unit, City Hospital, Birmingham, B18 7QH, UK
SOURCE: Clinical Science (1995), 89(3), 299-303
CODEN: CSCIAE; ISSN: 0143-5221
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyethylene glycol has been used extensively to measure small intestinal permeability in vivo. However, polyethylene glycol seems to traverse the intestinal mucosa in much greater quantities than sugar mols. of equivalent Mr. In addition, the recovery of the lowest Mr polymers of administered polyethylene glycol has been both low and unreliable. To compare the behavior of a range of polyethylene glycol polymers with sugar probes in vivo, a combined polyethylene glycol/mannitol/lactulose probe was administered sequentially to healthy individuals in the fasted state and under conditions of water-loading. Timed hourly urine collections were made for 6h. Mannitol and lactulose recoveries were all within the normal range and were unaffected by coadministration of water. The lactulose/mannitol recovery ratios did not vary significantly over the 6 h collection period. In contrast, the recovery of total polyethylene glycol was significantly greater when subjects were water-loaded. Furthermore, proportionally greater quantities of polyethylene glycol Mr 370 than Mr 854 were recovered towards the end of the collection period than at the start. Our results show that, in contrast to lactulose and mannitol, excretion of low-medium Mr polyethylene glycol polymers is highly dependent on coadministration of water. Furthermore, the differential rate of excretion of the low compared with the high Mr polyethylene glycol polymers suggests that the volume of distribution of the individual polymers may vary with Mr, and smaller polyethylene glycol mols. may undergo considerable renal tubular resorption.

L9 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:281710 CAPLUS
DOCUMENT NUMBER: 127:3275
TITLE: Size-dependent permeability of hydrophilic probes across rabbit colonic epithelium
AUTHOR(S): Ghandehari, Hamidreza; Smith, Philip L.; Ellens, Harma; Yeh, Ping-Yang; Kopecek, Jindrich
CORPORATE SOURCE: Dep. of Pharmaceutics and Pharmaceutical Chemistry/CCCD, University of Utah, Salt Lake City, UT, 84112, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 280(2), 747-753
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Colon-specific delivery of metabolically labile mols., such as proteins and peptides, is of particular interest in pharmaceutical research. Among the factors that may influence the permeability of drug mols. across

colonic mucosa are their mol. weight and geometry. The purpose of this study was to evaluate the influence of mol. geometry on in vitro permeability across rabbit distal colonic epithelia. Permeability of radiolabeled hydrophilic probes with different mol. wts. and geometries across isolated rabbit distal colonic tissue was evaluated by means of the Ussing chamber technique. The hydrodynamic radii of the probes (an indicator of mol. geometry) were estimated by theor. models as well as dynamic light scattering. The permeability studies were conducted in the presence and absence of the epithelial cells to evaluate the contribution of the underlying connective tissue to the overall in vitro permeability across the colonic mucosa. The rank order of the permeability of the markers was mannitol > lactulose > polyethylene glycol (PEG) 400 > PEG > PEG 900 > PEG 4000, which is consistent with their mol. wts. and estimated hydrodynamic radii. The permeability of inulin, a polyfructose mol. with a mol. weight of about 5000, however, was approx. the same as that of PEG 900 (mol. weight about 900). When the epithelial cells were removed, for the homologous series of PEGs, the permeabilities were proportional to their free diffusion coeffs. in water. It appears that for the PEG and lactulose probes, theor. estimation of the hydrodynamic radii, which assumes the mols. to be spherical in shape, provides a good basis for the dependence of permeability on geometry. The relatively high permeability of inulin seems to be due to its compact structure. The PEG permeability values in the absence of epithelial cells, in combination with their diffusion coeffs., indicate that the underlying connective tissue does not contribute to the overall permeability of these mols. across colonic mucosa in vitro.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:572332 CAPLUS
DOCUMENT NUMBER: 143:53579
TITLE: Composition and method for treatment of hepatic encephalopathy
INVENTOR(S): Halow, George M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005142099	A1	20050630	US 2003-748185	20031231
WO 2005065429	A2	20050721	WO 2005-US1	20050103
WO 2005065429	A3	20060223		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-748185 A 20031231

AB The inventions provide an improved treatment for hepatic encephalopathy characterized by hyperammonemia and/or constipation, comprising the oral

administration of polyethylene glycol (PEG) in amts. sufficient to reduce plasma levels of ammonia and/or to alleviate constipation. Preferably, the PEG is administered in combination with lactulose, which provides a palatable composition for the treatment of HE with excellent therapeutic benefits and reduced side effects as compared to lactulose alone.

L9 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:609889 CAPLUS
DOCUMENT NUMBER: 137:159344
TITLE: Polyethylene glycol coatings for effervescent granules with delayed effervescent effect
INVENTOR(S): Gergely, Gerhard; Gergely, Irmgard; Gergely, Thomas
PATENT ASSIGNEE(S): Australia
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6432450	B1	20020813	US 2000-656118	20000906
PRIORITY APPLN. INFO.:			US 2000-656118	20000906

AB The effervescent granules with delayed effervescent effect consist of at least one acid component and one component evolving gas under the action of acid, as well as of active substances, fragrances, plant exts., vitamins, minerals etc. admixed as needed, the particles of the acid component being coated with-preferably 1 to 30% by weight of-at least one carbonate compound-possibly including a partial reaction-and/or a hydrocolloid. The gas-evolving component consists of alkali hydrogen carbonate, alkali carbonate, and/or alkaline-earth carbonate particles which are coated with at least one further substance, particularly with a melt of polyethylene glycol 6000. The particles preferably have a grain size above 0.2 mm. For example, vitamin C effervescent granules with delayed effervescent effect contained (i) 1400 parts by weight of passivated acid component containing a mixt. of citric acid grit and calcium carbonate in which a partial reaction on the citric acid grit surface occurred, (ii) 980 parts by weight of the carbonate phase containing a mixt. of sodium hydrogen carbonate and calcium carbonate coated with melted polyethylene glycol, (iii) 180 parts by weight of ascorbic acid, and (iv) 934 parts by weight of sorbitol, as well as sweeteners and fragrances as needed. A dose of 3.6 g, which may be packed in long sachets, contains 180 mg of ascorbic acid and drops to the bottom when introduced into water. It is only 2 to 5 s later that the granules start to effervesce, and finally dissolve completely.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1975:475069 CAPLUS
DOCUMENT NUMBER: 83:75069
TITLE: Investigation of small bowel transit time in man utilizing pulmonary hydrogen (H2) measurements
AUTHOR(S): Bond, John H., Jr.; Levitt, Michael D.; Prentiss, Robin
CORPORATE SOURCE: Dep. Med., VA Hosp., Minneapolis, MN, USA
SOURCE: Journal of Laboratory and Clinical Medicine (1975), 85(4), 546-55
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Pulmonary H2 excretion was used to quantitate the small bowel transit time in man. This technique was based on the observation that H2 was produced when carbohydrate was fermented by colonic bacteria and that this H2 production was reflected by a concomitant increase in breath H2. The time between ingestion of the unabsorbable disaccharide lactulose and the rise in breath H2 represented the small intestinal transit time of the head of the lactulose load as it passed through the gut. Following ingestion of a mixt. of polyethylene glycol (PEG) and lactulose by 9 subjects, transit time measured by H2 excretion correlated closely with the simultaneously determined time for PEG to reach the distal ileum. The ileal appearance of PEG preceded the rise in H2 excretion by a mean of 7.6 min. Transit time of 10 g of lactulose in 40 healthy subjects averaged 72 min. Repeated studies in 6 subjects showed good individual reproducibility with subsequent measurements differing from initial by a mean of ±14%. There was an inverse relation between transit time and dose of lactulose ingested by 9 subjects with 5, 10, and 20 g lactulose having mean transit times of 128, 94, and 40 min, resp. This technique appears to provide a simple, safe, and noninvasive means of studying small bowel transit time in man.

L9 ANSWER 6 OF 25 EMBASE

ACCESSION NUMBER: 94246436 EMBASE
DOCUMENT NUMBER: 1994246436
TITLE: A study of colon preparation method for colonoscopy by using 500 ml of polyethylene glycol electrolyte lavage solution.
AUTHOR: Kanamori T.; Yokoyama Y.; Itoh M.; Takeuchi T.
CORPORATE SOURCE: I Department of Internal Medicine, Nagoya City University Med. School,Nagoya, Japan
SOURCE: Therapeutic Research, (1994) Vol. 15, No. SUPPL. 2, pp. 186-191. .
ISSN: 0289-8020 CODEN: THREEL
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 048 Gastroenterology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Sep 1994
Last Updated on STN: 14 Sep 1994

AB We have already reported the superiority of a colon preparation method (combined method) using polyethylene glycol electrolyte lavage solution (PEG-ELS) together with other laxatives to a method using only PEG-ELS. Of combined methods, the method using sodium picosulfate (10 ml) lactulose (90 ml), and PEG-ELS (1000 ml) has been excellent because of its high colon cleansing effect and good tolerance of patients. However, most patients have complained the distress of taking 1000 ml of PEG-ELS. Therefore we studied the usefulness of a new preparation method for colonoscopy by using 500 ml of PEG -ELS in terms of colon cleansing and patient acceptance. In this new method, 24 mg of sennoside was taken two days before examination, 10 ml of sodium picosulfate the day before, and 90 ml of lactulose and 500 ml of PEG-ELS on the day. In addition, the meals of the day before were restricted to bread or noodle, or other low residue diets. In colon cleansing effect, this new method has the same effect as our former method, i.e. about 171 (90.5%) of 189 cases were recognized as good colon cleansing effect. In patient tolerance, sixty (90.9%) of 66 patients who have experienced both methods within a year preferred to this new method. In conclusion, we appreciated that this is one of the best preparation methods for colonoscopy in terms of colon cleansing effect and patient

tolerance.

L9 ANSWER 7 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002140234 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11817992
TITLE: Economic impact of low dose polyethylene glycol 3350 plus electrolytes compared with lactulose in the management of idiopathic constipation in the UK.
AUTHOR: Christie Angela H; Culbert Pearl; Guest Julian F
CORPORATE SOURCE: Catalyst Health Economics Consultants, Northwood, Middlesex, United Kingdom.
SOURCE: PharmacoEconomics, (2002) Vol. 20, No. 1, pp. 49-60. Journal code: 9212404. ISSN: 1170-7690.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: (CLINICAL TRIAL)
(INTERVIEW)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Health Technology
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 7 Mar 2002
Last Updated on STN: 28 May 2002
Entered Medline: 24 May 2002

AB OBJECTIVE: To estimate the economic impact of using low dose polyethyene glycol 3350 (PEG 3350) plus electrolytes (PEG+E) compared with lactulose in the treatment of idiopathic constipation in ambulant patients. DESIGN AND PERSPECTIVE: This was a decision analytic modelling study performed from the perspective of the UK's National Health Service (NHS). METHODS: The clinical outcomes from a previously reported single-blind, randomised, multicentre trial were used as the clinical basis for the analysis. These data were combined with resource utilisation estimates derived from a panel of six general practitioners (GPs) and four nurses enabling a decision model to be constructed depicting the management of idiopathic constipation with either PEG+E or lactulose over 3 months. The model was used to estimate the expected 3-monthly NHS cost of using either laxative to manage idiopathic constipation. MAIN OUTCOME MEASURES AND RESULTS: The expected 3-monthly NHS cost of using PEG+E or lactulose to manage idiopathic constipation was estimated to be 85 pound sterling and 96 pound sterling per patient, respectively (1999/2000 values). However, significantly more patients were successfully treated with PEG+E than lactulose (53% versus 24%; $p < 0.001$) at 3 months. GP visits were the primary cost driver for both PEG +E- and lactulose-treated patients, accounting for 56% (2.9 visits) and 73% (4.4 visits), respectively, of the expected NHS cost per patient at 3 months. Among PEG+E-treated patients, the acquisition cost of PEG+E was the secondary cost driver, accounting for 30% of the expected NHS cost per patient at 3 months, whereas the acquisition cost of lactulose accounted for only 11% of the expected NHS cost per lactulose-treated patient. District nurse domiciliary visits accounted for 4% and thyroid function tests for 2%. The costs of switched laxatives, concomitant laxatives, and gastroenterologist and colorectal surgeon visits collectively accounted for up to 9% of the total. CONCLUSIONS: The true cost of managing idiopathic constipation is impacted on by a broad range of resources and not only laxative acquisition costs. This study indicated that managing idiopathic constipation with PEG+E instead of lactulose reduces the expected 3-monthly NHS cost by 11 pound sterling per patient. Moreover, using PEG+E instead of lactulose is expected to double the percentage of patients successfully treated at 3 months. Hence, PEG+E is a dominant treatment compared with

lactulose. This suggests that the decision to use either PEG+E or lactulose to treat idiopathic constipation should be based on efficacy, safety, patient preferences and total management costs, and not drug acquisition costs.

L9 ANSWER 8 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2006119037 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16505875
TITLE: [Nausea, vomiting and constipation in palliative care]. Kvalme, oppkast og obstipasjon i palliasjonsbehandling.
AUTHOR: Jordhoy Marit S; Aass Nina; Svensen Rune; Ervik Bente; Mohr Wenche
CORPORATE SOURCE: Enhet for kreft og lindrende behandling, Nordlandssykehuset, 8092 Bodo.. marit.jordhoy@nlsh.no
SOURCE: Tidsskrift for den Norske laegeforening, (2006 Feb 23) Vol. 126, No. 5, pp. 620-3. Ref: 20
Journal code: 0413423. E-ISSN: 0807-7096.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Norwegian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200603
ENTRY DATE: Entered STN: 1 Mar 2006
Last Updated on STN: 28 Mar 2006
Entered Medline: 27 Mar 2006

AB Nausea/vomiting and constipation are frequent symptoms among patients with advanced disease and short survival expectancy. The aim of this paper is to present the aetiology, diagnostic work-up, prophylaxis and treatment of these symptoms in palliative patients, based on a literature review and clinical experience. Nausea/vomiting is not a diagnosis, but symptoms with multiple causes. There is no universally applicable treatment approach. General guidelines for good treatment are: 1) impeccable assessment and work-up, 2) choice of treatment according to underlying causes and involved mechanisms, 3) pharmacological treatment applied jointly with non-pharmacological measures, 4) thorough follow-up and readjustment of treatment. During work-up, or if underlying causes can not be identified, metoclopramide, alternatively haloperidol, is the first drug of choice. Oral administration should be avoided until vomiting is controlled. Adequate hydration is important. The same general guidelines are applicable to handle constipation. However, prophylactic measures are also essential, focusing on risk factors (fluid intake, activity and toilet accommodations). Stool softening laxatives should be administered, (polyethylene glycol or lactulose), and if needed, combined with a bowel stimulant (bisacodyl or sodium picosulphate). Opioid use is among the most common causes of constipation and prescription of opioids should always be accompanied by prescription of laxatives. Exceptions are diarrhoea, ileostomy and dying patients.

L9 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:648411 CAPLUS
DOCUMENT NUMBER: 141:162415
TITLE: Intestinal environment controlling agent for oral use and normal intestinal flora growing kit for oral use
INVENTOR(S): Ito, Masaharu; Yamamoto, Kenji
PATENT ASSIGNEE(S): Ajinomoto Pharma Co., Ltd., Japan
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067037	A1	20040812	WO 2004-JP798	20040129

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRIORITY APPLN. INFO.: JP 2003-21610 A 20030130

AB It is intended to provide a composition for oral use aiming at eliminating harmful bacteria and controlling the proliferation ability of useful bacteria in the intestine and a kit for normalizing intestinal flora. As an intestinal environment controlling agent for oral use, a composition containing a gelatinous osmotic pressure controlling agent such as hardly digestible dextrin or polyethylene glycol and/or a crystalloid osmotic pressure controlling agent such as an electrolyte or a saccharide is employed. Then the intestinal environment controlling agent is combined with an intestinal useful bacterium composition and an intestinal useful bacterium growth promoter. For example, an intestinal environment controlling agent was formulated containing NaCl 2.93, KCl 1.49, NaHCO3 3.37, Na2SO4 11.37, and polyethylene glycol 117 g (dissolving in 2 L water for administration). An intestinal useful bacterium composition was formulated containing Enterococcus faecium culture powder 1, starch 0.9 g, and flavors q.s. An intestinal useful bacterium growth promoter was formulated containing agar 1.5, soy bean powder 1.5, apple fiber 0.5 g, and sugar q.s.

L9 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:796416 CAPLUS
DOCUMENT NUMBER: 139:307686
TITLE: Preparation of 2,3-diphenylpyridines as cannabinoid-1 receptor antagonists and inverse agonists
INVENTOR(S): Finke, Paul E.; Meurer, Laura C.; Debenham, John S.; Toupence, Richard B.; Walsh, Thomas F.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082191	A2	20031009	WO 2003-US9005	20030324
WO 2003082191	A3	20040115		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2479744	AA	20031009	CA 2003-2479744	20030324
AU 2003225964	A1	20031013	AU 2003-225964	20030324
EP 1492784	A2	20050105	EP 2003-745578	20030324

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US 2005182103	A1	20050818	US 2003-508043		20030324
JP 2005531520	T2	20051020	JP 2003-579734		20030324
PRIORITY APPLN. INFO.:			US 2002-368334P	P	20020328
			WO 2003-US9005	W	20030324

OTHER SOURCE(S): MARPAT 139:307686

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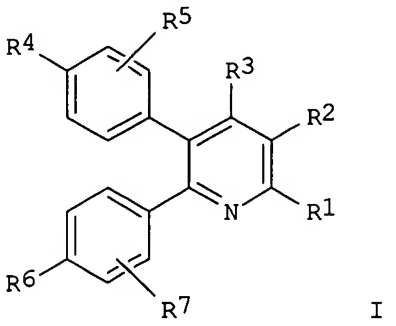

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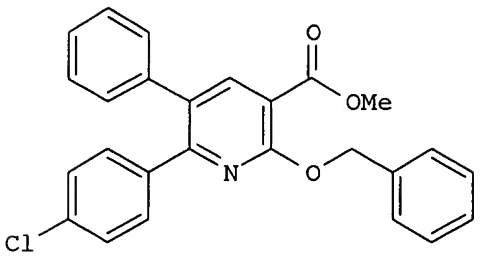

II

AB Title compds. I [wherein R1 = H, halo, CN, or (un)substituted alkyl, heterocycloalkyl(alkyl), heteroaryl, (hetero)arylalkyl, acyl, carboxy, (thio)ether, amino, carbamoyl, acylamino, carboxyamino, or ureido; R2 = H, CN, carboxy, halo, NO2, CF3, or (un)substituted carbamoyl; provided that R1 and R2 are not both H; R3 = H, CF3, or (un)substituted (cyclo)alkyl; R4-R7 = independently H, halo, amino, carboxy, alkyl, alkoxy, aryl(alkyl), OH, CF3, alkanoyloxy, or carbamoyloxy; provided that R6 and R7 are not both H; and pharmaceutically acceptable salts thereof] were prepared as cannabinoid-1 (CB1) receptor antagonists and/or inverse agonists (no data). For example, benzyl 4-chlorophenyl ketone was condensed with DMF dimethylacetal in DMF to give 3-(dimethylamino)-1-(4-chlorophenyl)-2-phenylprop-2-en-1-one. Cyclocondensation of the vinyl ketone with cyanoacetamide using NaH in DMF and MeOH provided the 3-cyano-2-pyridone. Conversion of the nitrile to the carboxylic acid with 50% H2SO4, followed by esterification using HCl in MeOH gave Me 6-(4-chlorophenyl)-5-phenyl-2-oxo-1,2-dihydropyridine-3-carboxylate. O-alkylation of the pyridone with benzyl bromide in the presence of Cs2CO3 in DMF afforded the title 2,3-diphenylpyridine II. Compds. of the invention and their pharmaceutical compns. serve as centrally acting drugs for the treatment, prevention, and suppression of diseases mediated by the CB1 receptor, such as psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuro-inflammatory disorders including multiple sclerosis and Guillain-Barre syndrome, the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, movement disorders, and schizophrenia (no

data). I are also useful for the treatment of substance abuse disorders, obesity or eating disorders, asthma, constipation, chronic intestinal pseudo-obstruction, and cirrhosis of the liver (no data).

L9 ANSWER 11 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2006221109 EMBASE
TITLE: Current mechanisms of action in treatment of chronic constipation and irritable bowel syndrome.
AUTHOR: Harris L.A.
CORPORATE SOURCE: Dr. L.A. Harris, Division of Gastroenterology and Hepatology, Mayo Clinic, 13400 East Shea Boulevard, Scottsdale, AZ 85259, United States. Harris.Lucinda@mayo.edu
SOURCE: Advanced Studies in Medicine, (2006) Vol. 6, No. 4 A, pp. S237-S242. .
Refs: 32
ISSN: 1530-3004 CODEN: ASMDCT
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jun 2006
Last Updated on STN: 8 Jun 2006

AB Patients with, chronic constipation and irritable bowel syndrome (IBS) have a variety of potential treatment options. Treatment typically begins with lifestyle changes and fiber supplementation. The predominant lifestyle changes are alteration of fluid intake, dietary modification, and physical activity. Laxatives constitute the second line of therapy. Patients can avail themselves of various emollient, osmotic, and stimulant laxatives. Among all the laxative agents, the strongest supporting evidence is for lactulose and polyethylene glycol. These conventional therapies have highly variable rates of therapeutic success. Most patients cope with their symptoms and are less than completely satisfied with therapy. Newer therapies have provided additional options that may help improve symptom relief and patient satisfaction. The 5-HT4 serotonin agonist tegaserod has demonstrated efficacy for chronic constipation and constipation-predominant IBS and is approved for treatment of men and women with chronic constipation and for women with IBS. The chloride channel activator lubiprostone recently was approved for treatment of constipation in men and women. The 5-HT(3) antagonist alosetron has approval for treatment of diarrhea-predominant IBS in women. A host of investigational agents are in various stages of evaluation and clinical development, many of which represent new approaches to treatment of chronic constipation and IBS.

L9 ANSWER 12 OF 25 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:77365 BIOSIS
DOCUMENT NUMBER: PREV200600084106
TITLE: Table To Toilet (TTT) program for management of chronic constipation and encopresis.
AUTHOR(S): Karjoo, Manoochehr; Kesselring, Shannon
SOURCE: Gastroenterology, (APR 2004) Vol. 126, No. 4, Suppl. 2, pp. A221.
Meeting Info.: Digestive Disease Week/105th Annual Meeting of the American-Gastroenterological-Association. New Orleans, LA, USA. May 16 -20, 2004. Amer Gastroenterol Assoc.

CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006

AB Chronic constipation and encopresis is one of the most common problems in Pediatrics. About 30-35 percent of daily clinic visits of pediatric gastroenterology consist of this problem. Most children have a history of taking multiple medications without improvement. The TTT program (Table To Toilet) was designed in our clinic With excellent results. This program includes that the patient go from the table to the toilet after meals and sit ten to twelve minutes. For children that have not been toilet trained, parents were instructed to hold the child in knee chest position while sitting on a chair. They were treated with a one-time enema if they had impaction followed by a stool softener (Polyethylene Glycol, Mineral oil, Lactulose) plus Senna extract. The stool softener and Senna were given together. This combination helps to maintain softness of stool while also helping with evacuation. The TTT program was instructed as mentioned above and each child was given a chary to record daily toileting. They were told that they might require hospitalization the next visit if they did not follow the instruction. This was mentioned so each would understand the seriousness of the problem and importance of treatment. All patients agreed to try their best. The medication was continued for at least one month regardless of improvement and continued even if the child was having regular bowel movements. From January 1999 to September 2003, 689 patients were seen with constipation and encopresis at our clinic. Of these, 492 had constipation and 197 with encopresis. These included 430 males and 259 females with the age range of 3 to 16 years. Ninety percent improved remarkably after 2 monthly visits when the), followed the medications and instructions. The others needed more visits for control of their problem. Recurrences happened if stopped medication early or refused to continue toileting. Conclusion: Behavior modification is TTT program will be helpful in the management of most patients with constipation and encopresis. Medication alone will result in temporary improvement while bowel-training results in complete resolution without recurrence, if continued toileting and without need of medications.

L9 ANSWER 13 OF 25 EMBASE
ACCESSION NUMBER: 2004438254 EMBASE
TITLE: [Coinfection HIV-HCV: Which therapeutic strategy is recommended?].
COINFECTION VIH-VHC: QUELLE PRISE EN CHARGE?.
AUTHOR: Aumaitre H.; Chauvet E.; Medus M.; Saada M.
CORPORATE SOURCE: H. Aumaitre, Serv. des Maladies Infect. et Trop., Centre Hospitalier Saint Jean, 66046 Perpignan, France. hugues.aumaitre@ch-perpignan.fr
SOURCE: Antibiotiques, (2004) Vol. 6, No. 3, pp. 151-163. .
Refs: 71
ISSN: 1294-5501 CODEN: ANTBFQ
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: French
SUMMARY LANGUAGE: French; English

ENTRY DATE: Entered STN: 28 Oct 2004
Last Updated on STN: 28 Oct 2004

AB Since the introduction of antiretroviral therapies in HIV patients, associated HCV infection has become the most important factor for therapeutic uses and for death rates. This evolution imposes the analysis of the serologic HCV status in all HIV positive patients. Besides serology tests, ARN dosage and determination of the genotype have become the bases of virologic status. It is only by means of liver biopsy and its pathology analysis that the evaluation of fibrosis degree and the decision for treatment can be established. The evaluation of the degree of severity of the hepatitis must also be based on biochemical tests and on the echography. Diverse factors of co-morbidity must be taken into account (alcoholism, hepatic steatosis, drug addictions) for the therapeutic decision. The duration of therapy is defined after several consecutive consultations showing that there is no major contra-indication, that the HIV treatment can be considered stable, and after having informed the patient on the objectives of the treatment, on its potential side effects for one year treatment. The combination PEG-interferon + ribavirin must be strictly controlled and adjusted as a function of tolerance. Monthly followed consultations permit patient training, and are in favour of successful treatment. Virologic curing is expected in 25 to 35% patients but non-responders must be seen regularly. Chronic treatments and new antiproteases are under evaluation. Cirrhotic patients (treated or not) should be seen at least once every 3 months and in case of the development of tumour or hepatic total failure they must be transferred to surgery teams. .COPYRGT. Masson, Paris, 2003.

L9 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:76274 CAPLUS
DOCUMENT NUMBER: 142:170087
TITLE: Method for treating irritable bowel syndrome using osmotic laxatives and fiber
INVENTOR(S): Pelham, Russell W.; Cleveland, Mark van Buren; Dipalma, Jack A.
PATENT ASSIGNEE(S): Braintree Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007170	A1	20050127	WO 2004-US22392	20040709
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004257742	A1	20050127	AU 2004-257742	20040709
CA 2531445	AA	20050127	CA 2004-2531445	20040709
US 2005152989	A1	20050714	US 2004-887684	20040709
EP 1663257	A1	20060607	EP 2004-756926	20040709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-485797P P 20030709
WO 2004-US22392 W 20040709

AB The invention provides a method for treating irritable bowel syndrome, comprising administering an osmotic laxative and fiber in a therapeutically effective regimen to a patient in need of such treatment. The therapeutically effective regimen includes administering the formulation in a dose and at a frequency and duration sufficient to reduce or eliminate the symptoms of irritable bowel syndrome or to provide symptomatic or palliative relief to the patient.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 25 EMBASE

ACCESSION NUMBER: 2005506543 EMBASE
TITLE: Guideline for chronic constipation management.
SOURCE: Journal of Family Practice, (2005) Vol. 54, No. 11, pp. 932. .
ISSN: 0094-3509 CODEN: JFAPDE
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Dec 2005
Last Updated on STN: 8 Dec 2005

AB This evidence-based guideline is based on a careful accompanying systematic review. Chronic constipation is defined as infrequent or difficult stool passage, incomplete evacuation, prolonged time to stool, or the need for manual maneuvers to pass stool, for at least 3 months. It is estimated that the prevalence of chronic constipation is approximately 15%; it is more common in women. Patients with alarm symptoms for cancer or bleeding should undergo a thorough diagnostic work-up. Otherwise, routine diagnostic testing is not recommended for patients with chronic constipation who have no alarm symptoms and no signs of organic disorder (such as hypothyroidism) after a careful history and physical examination. Regarding treatment: of the bulking agents, psyllium increases stool frequency but data are insufficient regarding calcium polycarbophil, methylcellulose, or bran. There is insufficient evidence regarding the efficacy of stool softeners or milk of magnesia. There is good evidence that polyethylene glycol and lactulose both improve stool frequency and consistency. There are few data regarding stimulant laxatives, but the available data suggest that they are of little benefit. Tegaserod (Zelnorm) improves the frequency and consistency of stools and reduces straining, particular in younger patients. There are insufficient data regarding alternative treatments, herbal supplements, lubricants, or combination laxatives.

L9 ANSWER 16 OF 25 EMBASE

ACCESSION NUMBER: 2004268588 EMBASE
TITLE: Current treatment options for chronic constipation.
AUTHOR: DiPalma J.A.
CORPORATE SOURCE: Dr. J.A. DiPalma, Division of Gastroenterology, University of South Alabama, College of Medicine, Mobile, AL, United States
SOURCE: Reviews in Gastroenterological Disorders, (2004) Vol. 4, No. SUPPL. 2, pp. S34-S42. .
Refs: 52
ISSN: 1533-001X CODEN: RGDEAK
COUNTRY: United States

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jul 2004
Last Updated on STN: 9 Jul 2004

AB Various agents are used for the medical management of chronic constipation but few have been carefully studied. This review examines available data concerning several bulk and fiber products, lubricating agents, stimulants, and osmotic laxatives, alone and in combination. Popular therapeutic options for initial treatment of chronic constipation are dietary fiber and medicinal bulk. Subsequent treatments if fiber is not successful or tolerated would include saline osmotic laxatives, lactulose, or stimulants like senna or bisacodyl. Recent data demonstrate polyethylene glycol laxative to be safe and effective as an initial or second-line agent for chronic constipation. Indications and use of surgery and biofeedback are also discussed. .COPYRGT. 2004 MedReviews, LLC.

L9 ANSWER 17 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005245900 EMBASE
TITLE: Medical treatment of constipation.
AUTHOR: Siegel J.D.; Di Palma J.A.
CORPORATE SOURCE: J.A. Di Palma, Gastroenterology Academic Offices, University of South Alabama, Knollwood Pavilion, 5600 Girby Rd., Mobile, AL 36693, United States. jdipalma@usouthal.edu
SOURCE: Clinics in Colon and Rectal Surgery, (2005) Vol. 18, No. 2, pp. 76-80. .
Refs: 36
ISSN: 1531-0043 CODEN: CCRSC
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2005
Last Updated on STN: 16 Jun 2005

AB Various agents are used for the medical management of chronic constipation, but few of these have been adequately studied. This article specifically examines the medical treatment of chronic constipation and the available data concerning bulk agents, lubricating agents, stimulants, and osmotic laxatives, used alone and in combination. Most experts consider dietary fiber or medicinal bulk agents to be the initial therapeutic option for the treatment of chronic constipation. If fiber is not successful or poorly tolerated, subsequent treatments may include saline osmotic laxatives, lactulose, 5-hydroxytryptamine4 (5-HT(4)) agonists (tegaserod), or stimulants such as senna or bisacodyl. Recent data also demonstrate both polyethylene glycol laxative and tegaserod to be safe and effective as initial therapy for chronic constipation. Copyright .COPYRGT. 2005 by Thieme Medical Publishers, Inc.

L9 ANSWER 18 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002439155 EMBASE
TITLE: Constipation in older people pharmacological management

issues.
AUTHOR: Woodward M.C.
CORPORATE SOURCE: M.C. Woodward, Aged Care Services, Austin and Repatriation Med. Center, Repatriation Campus, Banksia Street, Heidelberg West, Vic. 3081, Australia. michael.woodward@armc.org.au
SOURCE: Journal of Pharmacy Practice and Research, (2002) Vol. 32, No. 1, pp. 37-43. .
Refs: 62
ISSN: 1445-937X CODEN: JPPRBR
COUNTRY: Australia
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 020 Gerontology and Geriatrics
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 Dec 2002
Last Updated on STN: 27 Dec 2002

AB Constipation is a common complaint amongst older people although they are often concerned about features of constipation other than bowel action frequency. A careful assessment should be made, including a history, examination and appropriate investigations. Non-pharmacological management often avoids the use of laxatives and includes adequate fibre, fluid and exercise. The laxatives most appropriate for older people include stimulants such as senna, bulking agents and osmotic agents such as polyethylene glycol plus electrolytes or sorbitol.
Short-term use is nearly always sufficient. Faecal impaction should be sought and managed before giving oral agents. Enemas and suppositories are usually appropriate for impaction and for excessive straining. Management of constipation with these measures will avoid long-term use and abuse of laxatives.

L9 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105

US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L9 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 85258842 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4018502
TITLE: Effects of morphine and atropine on motility and transit in the human ileum.
AUTHOR: Borody T J; Quigley E M; Phillips S F; Wienbeck M; Tucker R L; Haddad A; Zinsmeister A R
CONTRACT NUMBER: AM32121 (NIADDK)
AM34988 (NIADDK)
RR00585 (NCRR)
SOURCE: Gastroenterology, (1985 Sep) Vol. 89, No. 3, pp. 562-70.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198509
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 29 Jan 1999
Entered Medline: 12 Sep 1985

AB We examined motility of the ileocecal region, pressures at the ileocecal sphincter, and ileal flow after therapeutic doses of morphine and atropine. Using a factorial design in two cells of 8 (2(3] subjects, drugs were given during fasting and postcibally. Morphine (100 micrograms/kg body wt as a bolus intravenously) and atropine (7 micrograms/kg body wt as a bolus) stimulated migrating bursts of phasic activity (similar to phase III of the migrating motor complex). Morphine initially stimulated ileal flow, but atropine could not be shown to have this effect. Atropine reduced markedly the occurrence of sporadic pressure waves in the ileum, but morphine did not. Whereas atropine delayed mouth-to-ileum transit of polyethylene glycol, given in a mixed meal, morphine did not. Naloxone, in the dosage used (40 micrograms/kg body wt as a bolus, followed by 10 micrograms/kg body wt X h) had no independent effects on motility or flow, but did blunt the stimulatory effects of morphine and atropine on migrating motor complexes. We could not demonstrate an effect of any drug on the transit of lactulose from terminal ileum to cecum. Neither morphine nor atropine had impressive effects on tone at the ileocecal sphincter. These observations, while not specifying the mechanisms for constipation after opiates or anticholinergics, highlight

the complexities of small bowel transit in humans and point out that the antidiarrheal effects of drugs are probably multifactorial.

L9 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:10262 CAPLUS
DOCUMENT NUMBER: 136:90945
TITLE: Preparation of stable pharmaceutical compositions
INVENTOR(S): Busson, Patrick; Schroeder, Marco
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000201	A2	20020103	WO 2001-EP6834	20010618
WO 2002000201	A3	20020418		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2411153	AA	20020103	CA 2001-2411153	20010618
EP 1296656	A2	20030402	EP 2001-960323	20010618
EP 1296656	B1	20060802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012014	A	20030513	BR 2001-12014	20010618
JP 2004501184	T2	20040115	JP 2002-504983	20010618
NZ 523024	A	20040827	NZ 2001-523024	20010618
RU 2244542	C2	20050120	RU 2003-100506	20010618
US 2002018812	A1	20020214	US 2001-891069	20010625
US 6534087	B2	20030318		
US 2003039614	A1	20030227	US 2002-266363	20021008
US 7074431	B2	20060711		
ZA 2002009649	A	20040310	ZA 2002-9649	20021127
NO 2002006197	A	20021223	NO 2002-6197	20021223
HK 1058314	A1	20060324	HK 2004-101186	20040219
US 2006134205	A1	20060622	US 2006-354716	20060215

PRIORITY APPLN. INFO.:

EP 2000-113535	A	20000627
WO 2001-EP6834	W	20010618
US 2001-891069	A1	20010625
US 2002-266363	A3	20021008

AB The present invention relates to a method for the preparation of pharmaceutical compns., in the form of expanded, mech. stable, lamellar, porous, sponge-like or foam structures out of solns. and dispersions. This method comprises the steps of preparing a solution or a homogeneous dispersion of a liquid and a compound selected from the group consisting of 1 or more drugs, 1 or more excipients, and mixts., followed by the expansion of the solution or the homogeneous dispersion without boiling. The invention also relates to the compns., their further processing and any corresponding dosage forms obtainable by the above method. Thus, a composition contained oseltamivir 10.0, polymethacrylate 90.0, and isopropanol 80.0%.

L9 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:891450 CAPLUS

DOCUMENT NUMBER: 134:46798
TITLE: Contact lens and ophthalmic solutions
INVENTOR(S): De, Bruiju Chris; Christ, F. Richard; Dziabo, Anthony J.; Vigh, Joseph
PATENT ASSIGNEE(S): Ndt, Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6162393	A	20001219	US 1998-130542	19980806
CA 2339635	AA	20000217	CA 1999-2339635	19990805
EP 1102602	A1	20010530	EP 1999-940927	19990805
EP 1102602	B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002522120	T2	20020723	JP 2000-563316	19990805
EP 1336415	A2	20030820	EP 2003-11083	19990805
EP 1336415	A3	20040728		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AU 764906	B2	20030904	AU 1999-54686	19990805
AT 264697	E	20040515	AT 1999-940927	19990805
US 6793941	B1	20040921	US 2000-711784	20001113
US 2003086986	A1	20030508	US 2002-117533	20020404

PRIORITY APPLN. INFO.:

US 1998-130542	A	19980806
EP 1999-940927	A3	19990805
WO 1999-US17853	W	19990805
US 2000-711784	A2	20001113

AB Benzyldimethyl {2-[2-(p-1,1,3,3-tetramethylbutylphenoxy)ethoxy]ethyl} ammonium chloride (BDT) forms the basis of contact lens solns. that are unusually effective at reducing the number and wide variety of pathogenic microorganisms that may infect rigid gas permeable or soft contact lenses. Furthermore, it has been discovered that natural occurring compds. alone and in combination with chemical agents can be used in ophthalmic solns. such as contact lens solution to enhance and complement their antimicrobial, cleaning and wetting activity or to reduce irritation to the eye. The basic contact lens solution comprises an effective concentration of BDT (preferably 1 to 100 ppm), with naturally occurring plant products possessing activities complementary to BDT, in an isotonic diluent buffered with a physiol. acceptable buffer to a physiol. natural range.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 25 EMBASE
ACCESSION NUMBER: 2005245907 EMBASE
TITLE: Childhood constipation: Evaluation and management.
AUTHOR: Pashankar D.S.
CORPORATE SOURCE: Dr. D.S. Pashankar, Yale University School of Medicine, Section of Pediatric Gastroenterology/Hepatology, FMP 408, 333 Cedar St., New Haven, CT 06520, United States. dinesh.pashankar@yale.edu
SOURCE: Clinics in Colon and Rectal Surgery, (2005) Vol. 18, No. 2, pp. 120-127. .
Refs: 37
ISSN: 1531-0043 CODEN: CCRSC
COUNTRY: United States

DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jun 2005
Last Updated on STN: 16 Jun 2005

AB Constipation is a common problem in children. It is also a long-term problem persisting for many months to years in children. Approximately 95% of childhood constipation is functional in nature without any obvious cause. Evaluation of a child with constipation requires a thorough history and physical examination. Hirschsprung's disease is an important cause of constipation arising in infancy and requires a thorough diagnostic evaluation and surgical treatment. Treatment of functional constipation in children requires a well-designed plan and a team approach involving the child, parents, and a health care provider. Treatment involves education of the family about constipation and encopresis, fecal disimpaction, and long-term maintenance therapy of laxatives and behavioral modification. Laxatives such as magnesium hydroxide, lactulose, and mineral oil have been used in children for a long time. A new laxative, polyethylene glycol 3350, has been used successfully in children with constipation and encopresis. Several novel therapeutic interventions have been tried for children presenting with intractable constipation, refractory to conventional treatment.

L9 ANSWER 24 OF 25 EMBASE
ACCESSION NUMBER: 2004529206 EMBASE
TITLE: The treatment of chronic constipation in elderly people: An update.
AUTHOR: Bosshard W.; Dreher R.; Schnegg J.-F.; Bula C.J.
CORPORATE SOURCE: Dr. C.J. Bula, CUTR Sylvana, Ch de Sylvana 10, 1066 Epalinges, Lausanne, Switzerland. christophe.bula@chuv.hospvd.ch
SOURCE: Drugs and Aging, (2004) Vol. 21, No. 14, pp. 911-930. .
Refs: 113
ISSN: 1170-229X CODEN: DRAGE6
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Dec 2004
Last Updated on STN: 30 Dec 2004

AB Constipation is a common problem in elderly persons, with prevalence ranging from 15% to 20% in the community-dwelling elderly population and up to 50% in some studies of nursing home residents. In these patients, constipation results from a combination of risk factors, such as reduced fibre and fluid intake, decreased physical activity resulting from chronic diseases and multiple medications. Despite the high prevalence of constipation, there is surprisingly little evidence available on which to base management decisions of this common condition. Increased fluid intake, regular physical activity and high fibre intake are usually proposed as first step nonpharmacological measures. However, adherence to these measures is limited and pharmacological treatment is frequently required. Data are too limited, especially in elderly persons, to formally recommend one class of laxatives over another or one agent over

another within each class. However, bulk-forming and osmotic laxatives are usually recommended as first-line agents, even though data on their effectiveness are limited. The need to maintain good hydration is a limitation in the use of bulk-forming laxatives, in particular, in frail elderly patients. In these patients, polyethylene glycol, an osmotic agent, is an attractive alternative. In addition, it has been shown to relieve faecal impaction in frail patients with neurological disease. Its cost and potential, danger in patients at high risk for aspiration is, however, a limitation. Stimulant laxatives are considered mainly as an intermittent treatment in patients who do not respond to bulk-forming or osmotic laxatives. Several promising compounds such as the new serotonin 5-HT(4) receptor agonists (tegaserod, prucalopride) and neurotrophin-3 (NT3) have not been adequately tested in older individuals. They are not routinely used and their role in the management of constipation in these patients will be more precisely defined in the future. Other treatment options are available (acupuncture, biofeedback, botulinum toxin and surgery), but experience with these interventions in elderly patients is limited and their indications in this population remain to be clarified. Management of constipation in elderly persons depends largely on experience and beliefs. Several new compounds seem promising but will need to be specifically tested in this population before being recommended.

L9 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004284709 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15184812
TITLE: Current treatment options for chronic constipation.
AUTHOR: DiPalma Jack A
CORPORATE SOURCE: Division of Gastroenterology, University of South Alabama College of Medicine, Mobile, Alabama, USA.
SOURCE: Reviews in gastroenterological disorders, (2004) Vol. 4 Suppl 2, pp. S34-42.
Journal code: 101140143. ISSN: 1533-001X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 9 Jun 2004
Last Updated on STN: 29 Sep 2004
Entered Medline: 28 Sep 2004

AB Various agents are used for the medical management of chronic constipation but few have been carefully studied. This review examines available data concerning several bulk and fiber products, lubricating agents, stimulants, and osmotic laxatives, alone and in combination. Popular therapeutic options for initial treatment of chronic constipation are dietary fiber and medicinal bulk. Subsequent treatments if fiber is not successful or tolerated would include saline osmotic laxatives, lactulose, or stimulants like senna or bisacodyl. Recent data demonstrate polyethylene glycol laxative to be safe and effective as an initial or second-line agent for chronic constipation. Indications and use of surgery and biofeedback are also discussed.

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=> s (encephalopathy (l) (hepatic or portosystemic or hepatocerebral or
portal-systemic or portosystemic)
UNMATCHED LEFT PARENTHESIS '(ENCEPHALOP'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s encephalopathy (l) (hepatic or portosystemic or hepatocerebral or
portal-systemic or portosystemic)
L10      22646 ENCEPHALOPATHY (L) (HEPATIC OR PORTOSYSTEMIC OR HEPATOCEREBRAL
               OR PORTAL-SYSTEMIC OR PORTOSYSTEMIC)

=> s l10 or hepatic coma or hepatic stupor
L11      25277 L10 OR HEPATIC COMA OR HEPATIC STUPOR

=> d his

     (FILE 'HOME' ENTERED AT 22:38:41 ON 16 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 22:39:02 ON 16 AUG 2006
L1           13 S LACTULOSE
L2         7708 S POLYETHYLENE GLYCOL
L3           69 S L2 AND PEG

     FILE 'MEDLINE' ENTERED AT 22:41:19 ON 16 AUG 2006

     FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 22:43:26 ON 16 AUG 2006
L4         9940 S 4618-18-2/RN OR LACTULOSE OR CEPHULAC OR 576-08-9/RN OR 29319
L5          231 S L4 AND (PEG OR POLYETHYLENE GLYCOL)
L6          129 DUP REM L5 (102 DUPLICATES REMOVED)
L7          129 FOCUS L6 1-
L8           25 S L7 AND (COMBO? OR COMBI? OR TOGETHER OR COADMINI? OR CO-ADMI
L9           25 FOCUS L8 1-
L10       22646 S ENCEPHALOPATHY (L) (HEPATIC OR PORTOSYSTEMIC OR HEPATOCEREBRA
L11       25277 S L10 OR HEPATIC COMA OR HEPATIC STUPOR

=> s l4 and l11
L12       1283 L4 AND L11

=> s l11 and (peg or polyethylene glycol)
L13         26 L11 AND (PEG OR POLYETHYLENE GLYCOL)

=> s l12 and l13
L14          7 L12 AND L13

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           6 DUP REM L14 (1 DUPLICATE REMOVED)

=> focus
PROCESSING COMPLETED FOR L15
L16           6 FOCUS L15 1-

=> d ibib abs it 1-6

L16  ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:572332  CAPLUS
DOCUMENT NUMBER:          143:53579
TITLE:                    Composition and method for treatment of
                          hepatic encephalopathy
INVENTOR(S):              Halow, George M.
PATENT ASSIGNEE(S):       USA
```

SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005142099	A1	20050630	US 2003-748185	20031231
WO 2005065429	A2	20050721	WO 2005-US1	20050103
WO 2005065429	A3	20060223		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-748185 A 20031231

AB The inventions provide an improved treatment for hepatic encephalopathy characterized by hyperammonemia and/or constipation, comprising the oral administration of polyethylene glycol (PEG) in amts. sufficient to reduce plasma levels of ammonia and/or to alleviate constipation. Preferably, the PEG is administered in combination with lactulose, which provides a palatable composition for the treatment of HE with excellent therapeutic benefits and reduced side effects as compared to lactulose alone.

IT Blood plasma
Human
(composition and method for treatment of hepatic encephalopathy)

IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)

IT Intestine, disease
(constipation; composition and method for treatment of hepatic encephalopathy)

IT Powders
(dry; composition and method for treatment of hepatic encephalopathy)

IT Brain, disease
(hepatic encephalopathy; composition and method for treatment of hepatic encephalopathy)

IT Drug delivery systems
(oral; composition and method for treatment of hepatic encephalopathy)

IT Drug delivery systems
(solids; composition and method for treatment of hepatic encephalopathy)

IT 4618-18-2, Lactulose
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)

IT 25322-68-3, Polyethylene glycol

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)

IT 7664-41-7, Ammonia, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperammonemia; composition and method for treatment of hepatic encephalopathy)

L16 ANSWER 2 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005066408 EMBASE
TITLE: [New drugs for old problems: Constipation and polyethylene glycol].
NUOVI FARMACI PER VECCHI PROBLEMI: STIPSI E POLIETILENGLICOLE.
AUTHOR: Fontana M.; Martelli L.; Condo V.
CORPORATE SOURCE: M. Fontana, Unita Operativa di Pediatria, Ospedale dei Bambini Vittore Buzzi, Milano, Italy
SOURCE: Medico e Bambino, (31 Dec 2004) Vol. 23, No. 11, pp. 706-711. .
Refs: 35
ISSN: 1591-3090 CODEN: MBAMFC
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
039 Pharmacy
LANGUAGE: Italian
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 2005
Last Updated on STN: 24 Feb 2005

AB Drugs which are commonly used to soften the stools include mineral oils and osmotic laxatives. While the former are not recommended in paediatric patients, the latter, such as lactulose and lactitol, which are equivalent, must be given at significantly higher dosage than recommended by Italian manufacturers and their effect is at least partially due to modification of bacterial flora. Polyethylene glycols (PEG) are molecules of diverse weight which cannot be absorbed nor metabolized. PEG (either PEG 3350 or PEG 4000), at the concentration of 7.1 percent keeps the accompanying water in the intestine without any further drawing in of water from the intestinal wall, thus avoiding the risk of dehydration. High volumes of PEG can be used for complete intestinal lavage, as for colonoscopy, or for treating severe foecal impaction. Low volumes, on average 1 g/kg/die, i.e. 15 ml/kg/die solution to be increased or reduced depending on effect, are effective in the great majority of cases for treating chronic constipation. In PEG products manufactured in Italy salts give an unpleasant flavour which is not present in a product recently marketed in the US, which contains only pure PEG.

L16 ANSWER 3 OF 6 MEDLINE on STN

ACCESSION NUMBER: 2005086809 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15716622
TITLE: Neostigmine for the treatment of acute hepatic encephalopathy with acute intestinal pseudo-obstruction in a cirrhotic patient.
AUTHOR: Park Chang Hwan; Joo Young Eun; Kim Hyun Soo; Choi Sung Kyu; Rew Jong Sun; Kim Sei Jong
CORPORATE SOURCE: Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea.
SOURCE: Journal of Korean medical science, (2005 Feb) Vol. 20, No.

1, pp. 150-2.
Journal code: 8703518. ISSN: 1011-8934.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 18 Feb 2005
Last Updated on STN: 12 Jul 2005
Entered Medline: 11 Jul 2005

AB We treated a 49-yr-old man with neostigmine, who had liver cirrhosis, acute hepatic encephalopathy, and acute intestinal pseudoobstruction. He was admitted in a state of hepatic confusion. On physical examination, the abdomen was distended; and bowel sound was absent. Plain abdomen film revealed multiple air-fluid levels and distention of bowel loops. Initially, we gave him lactulose enemas every 6 hr for one day without improvement in his mental state. Furthermore, he became to a state of coma. Therefore, we gave him 0.5 mg of neostigmine subcutaneously to improve his peristaltic movement, and 2 L of polyethylene glycol electrolyte solution through a nasogastric tube for 4 hr to reduce the production and absorption of gut-derived toxins of nitrogenous compounds. After these treatments, the venous ammonia level decreased to the normal range within 12 hr, and the coma disappeared after 2 days. We suggest that neostigmine may be one of the most effective treatments to initiate peristaltic movement and bowel cleansing in cirrhotic patients with acute hepatic encephalopathy and acute intestinal pseudoobstruction.

L16 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:311325 BIOSIS
DOCUMENT NUMBER: PREV199598325625
TITLE: Use of polyethylene glycol 4000 for the treatment of posthemorrhagic encephalopathy.
AUTHOR(S): Roblin, Xavier; Blais, Jacques; Legrand, Christope; Andre, Francois; Pothin, Agnes
CORPORATE SOURCE: Serv. Hepato-Gastroenterol., CHD Felix-Guyon, F-97405 Saint-Denis, La Reunion, France
SOURCE: Gastroenterologie Clinique et Biologique, (1994) Vol. 18, No. 12, pp. 1146.
CODEN: GCBIDC. ISSN: 0399-8320.
DOCUMENT TYPE: Letter
LANGUAGE: French
ENTRY DATE: Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995

IT Major Concepts
Behavior; Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Nervous System (Neural Coordination); Pharmacology; Psychiatry (Human Medicine, Medical Sciences); Toxicology
IT Chemicals & Biochemicals
POLYETHYLENE GLYCOL 4000; MANNITOL; LACTULOSE; ALCOHOL
IT Miscellaneous Descriptors
ALCOHOL CONSUMPTION; BLAKEMORE TUBE; CASE STUDY; CIRRHOSIS; GASTROINTESTINAL HEMORRHAGE; HEPATIC ENCEPHALOPATHY ; LACTULOSE; MANNITOL; POLYETHYLENE GLYCOL 4000
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name

human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 69-65-8Q (MANNITOL)
87-78-5Q (MANNITOL)
4618-18-2 (LACTULOSE)
64-17-5 (ALCOHOL)
25322-68-3 (POLYETHYLENE GLYCOL 4000)

L16 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:317826 BIOSIS
DOCUMENT NUMBER: PREV199598332126
TITLE: Is the treatment of acute hepatic encephalopathy justified in cirrhosis?.
AUTHOR(S): Doffoel, Michel [Reprint author]; Vetter, Denis
CORPORATE SOURCE: Serv. Hepato-Gastroenterol., Hopital Civil, F-67091 Strasbourg Cedex, France
SOURCE: Gastroenterologie Clinique et Biologique, (1994) Vol. 18, No. 12, pp. 1055-1056.
CODEN: GCBIDC. ISSN: 0399-8320.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: French
ENTRY DATE: Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995
IT Major Concepts
Behavior; Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Infection; Mathematical Biology (Computational Biology); Metabolism; Nervous System (Neural Coordination); Pharmacology; Psychiatry (Human Medicine, Medical Sciences); Toxicology
IT Chemicals & Biochemicals
LACTULOSE; NEOMYCIN; BENZODIAZEPINE; MANNITOL; POLYETHYLENE GLYCOL
IT Miscellaneous Descriptors
ANASTOMOSIS; ANTIBIOTIC THERAPY; BACTERIAL INFECTION; BENZODIAZEPINE; DIGESTIVE HEMORRHAGE; DISACCHARIDE; ETIOLOGY; HEPATOCELLULAR INSUFFICIENCY; HYDROELECTROLYTIC DISORDER; LACTULOSE; MANNITOL; NEOMYCIN; NEUROPSYCHIATRIC MANIFESTATION; POLYETHYLENE GLYCOL; STATISTICAL ANALYSIS; TOXICITY
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 4618-18-2 (LACTULOSE)
1404-04-2 (NEOMYCIN)
12794-10-4 (BENZODIAZEPINE)
69-65-8Q (MANNITOL)
87-78-5Q (MANNITOL)
25322-68-3 (POLYETHYLENE GLYCOL)

L16 ANSWER 6 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004438254 EMBASE
TITLE: [Coinfection HIV-HCV: Which therapeutic strategy is recommended?].
COINFECTION VIH-VHC: QUELLE PRISE EN CHARGE?.
AUTHOR: Aumaitre H.; Chauvet E.; Medus M.; Saada M.
CORPORATE SOURCE: H. Aumaitre, Serv. des Maladies Infect. et Trop., Centre

Hospitalier Saint Jean, 66046 Perpignan, France.
hugues.aumaitre@ch-perpignan.fr
SOURCE: Antibiotiques, (2004) Vol. 6, No. 3, pp. 151-163. .
Refs: 71
ISSN: 1294-5501 CODEN: ANTBFQ
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: French
SUMMARY LANGUAGE: French; English
ENTRY DATE: Entered STN: 28 Oct 2004
Last Updated on STN: 28 Oct 2004
AB Since the introduction of antiretroviral therapies in HIV patients, associated HCV infection has become the most important factor for therapeutic uses and for death rates. This evolution imposes the analysis of the serologic HCV status in all HIV positive patients. Besides serology tests, ARN dosage and determination of the genotype have become the bases of virologic status. It is only by means of liver biopsy and its pathology analysis that the evaluation of fibrosis degree and the decision for treatment can be established. The evaluation of the degree of severity of the hepatitis must also be based on biochemical tests and on the echography. Diverse factors of co-morbidity must be taken into account (alcoholism, hepatic steatosis, drug addictions) for the therapeutic decision. The duration of therapy is defined after several consecutive consultations showing that there is no major contra-indication, that the HIV treatment can be considered stable, and after having informed the patient on the objectives of the treatment, on its potential side effects for one year treatment. The combination PEG-interferon + ribavirin must be strictly controlled and adjusted as a function of tolerance. Monthly followed consultations permit patient training, and are in favour of successful treatment. Virologic curing is expected in 25 to 35% patients but non-responders must be seen regularly. Chronic treatments and new antiproteases are under evaluation. Cirrhotic patients (treated or not) should be seen at least once every 3 months and in case of the development of tumour or hepatic total failure they must be transferred to surgery teams. .COPYRGT. Masson, Paris, 2003.

=>

L18 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:572332 CAPLUS
DOCUMENT NUMBER: 143:53579
TITLE: Composition and method for treatment of hepatic encephalopathy
INVENTOR(S): Halow, George M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005142099	A1	20050630	US 2003-748185	20031231
WO 2005065429	A2	20050721	WO 2005-US1	20050103
WO 2005065429	A3	20060223		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-748185 A 20031231

AB The inventions provide an improved treatment for hepatic encephalopathy characterized by hyperammonemia and/or constipation, comprising the oral administration of polyethylene glycol (PEG) in amts. sufficient to reduce plasma levels of ammonia and/or to alleviate constipation. Preferably, the PEG is administered in combination with lactulose, which provides a palatable composition for the treatment of HE with excellent therapeutic benefits and reduced side effects as compared to lactulose alone.

IT Blood plasma
Human
(composition and method for treatment of hepatic encephalopathy)

IT Polyoxyalkylenes, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)

IT Intestine, disease
(constipation; composition and method for treatment of hepatic encephalopathy)

IT Powders
(dry; composition and method for treatment of hepatic encephalopathy)

IT Brain, disease
(hepatic encephalopathy; composition and method for treatment of hepatic encephalopathy)

IT Drug delivery systems
(oral; composition and method for treatment of hepatic encephalopathy)

IT Drug delivery systems
(solids; composition and method for treatment of hepatic

encephalopathy)
IT 4618-18-2, Lactulose
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)
IT 25322-68-3, Polyethylene glycol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition and method for treatment of hepatic encephalopathy)
IT 7664-41-7, Ammonia, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hyperammonemia; composition and method for treatment of hepatic encephalopathy)

L18 ANSWER 2 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003300848 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12828094
TITLE: Neostigmine and polyethylene glycol electrolyte solution for the therapy of acute hepatic encephalopathy with liver cirrhosis and ascites.
AUTHOR: Kiba Takayoshi; Numata Kazushi; Saito Satoru
CORPORATE SOURCE: Third Department of Internal Medicine, Yokohama City University School of Medicine, 3-9 Fukuura, Kanazawa-ku, Yokohama 236, Japan.. takkiba@hotmail.com
SOURCE: Hepato-gastroenterology, (2003 May-Jun) Vol. 50, No. 51, pp. 823-6.
Journal code: 8007849. ISSN: 0172-6390.
PUB. COUNTRY: Greece
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 28 Jun 2003
Last Updated on STN: 24 Oct 2003
Entered Medline: 23 Oct 2003
AB We treated a 75-year-old man who had non-B and non-C, and Child's class C liver cirrhosis and acute hepatic encephalopathy with neostigmine and polyethylene glycol electrolyte solution. He received repeated transcatheter artrial embolization and percutaneous ethanol injection combination therapy for multiple hepatocellular carcinomas, which controlled his disease for 25 months from the first treatment. He was admitted in a state of hepatic coma after being found unresponsive at his home. With the consent of the patient's family, we gave him 1.0 mg of neostigmine intramuscularly to improve his peristaltic movement, and 2 L of polyethylene glycol electrolyte solution through a nasogastric tube for 4 hours to reduce the production and absorption of gut-derived toxins of nitrogenous compounds. Using these treatments, the blood ammonia level decreased to the normal range within 8 hours, and the coma disappeared after 2 days. We suggest that a combination approach of neostigmime and polyethylene glycol electrolyte solution may be one of the most effective treatments for acute hepatic encephalopathy associated with liver cirrhosis and ascites.

L18 ANSWER 3 OF 19 MEDLINE on STN
ACCESSION NUMBER: 95269927 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7750690
TITLE: [Use of polyethylene glycol 4000 in hepatic encephalopathy related to

digestive hemorrhages].
Utilisation du polyethylene glycol 4000
dans l'encephalopathie hepatique liee aux hemorragies
digestives.
AUTHOR: Roblin X; Blais J; Legrand C; Andre F; Pothin A
SOURCE: Gastroenterologie clinique et biologique, (1994) Vol. 18, No. 12, pp. 1146.
Journal code: 7704825. ISSN: 0399-8320.
PUB. COUNTRY: France
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 29 Jun 1995
Last Updated on STN: 29 Jun 1995
Entered Medline: 20 Jun 1995

L18 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:40281 CAPLUS
DOCUMENT NUMBER: 114:40281
TITLE: Early changes in the permeability of the blood-brain barrier produced by toxins associated with liver failure
AUTHOR(S): McClung, H. Juhling; Sloan, Howard R.; Powers, Priscilla; Merola, A. John; Murray, Robert; Kerzner, Benny; Pollack, J. Dennis
CORPORATE SOURCE: Dep. Pediatr., Child. Hosp. Columbus, Columbus, OH, 43205, USA
SOURCE: Pediatric Research (1990), 28(3), 227-31
CODEN: PEREBL; ISSN: 0031-3998
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was designed to determine whether substances that appear in the serum during the course of liver failure have a detrimental effect on the passive permeability of the blood-brain [blood-cerebrospinal fluid (CSF)] barrier. Lactic acid, octanoic acid, and ammonia were infused into rabbits for 4 h. The permeability changes of the blood-brain barrier were quantified by infusing polyethylene glycol 400 (PEG 400) and measuring the quantity and average mol wt of the PEG 400 that entered the CSF. The lipid solubility and effective diffusional radius of the PEG mols. were also quantified to provide greater precision for measurements using this probe. None of the animals receiving toxic infusions became seriously ill during the infusions. Low dose infusions of lactic acid, octanoic acid, and ammonia increased the effective pore diameter of the blood-brain barrier from 7.3 Å to an average of 8.5 Å. The amount of PEG entering the CSF increased from 1.7 to 4.0, 4.7, and 6.7 mmol/L, resp. Rabbits with galactosamine-induced liver failure had 10.1 mmol/L PEG 400 in the CSF before any evidence of cerebral edema. These changes occur soon after these toxins accumulate in the plasma and may alone or together with other toxins account for the permeability changes that allow neurotoxic substances to enter the brain during hepatic disease and encephalopathies such as Reye's syndrome.
IT Blood-brain barrier
(liver failure-associated toxins of blood serum effects on permeability of)
IT Blood serum
(liver failure-associated toxins of, blood-brain barrier permeability response to)
IT Toxins
RL: BIOL (Biological study)
(liver failure-associated, of blood serum, blood-brain barrier

permeability response to)
IT Liver, disease or disorder
(failure, toxins of blood serum associated with, blood-brain barrier permeability response to)
IT 50-21-5, Lactic acid, biological studies 124-07-2, Octanoic acid, biological studies 7664-41-7, Ammonia, biological studies
RL: BIOL (Biological study)
(liver failure-associated, of blood serum, blood-brain barrier permeability response to)

L18 ANSWER 5 OF 19 EMBASE
ACCESSION NUMBER: 2005066408 EMBASE
TITLE: [New drugs for old problems: Constipation and polyethylene glycol].
NUOVI FARMACI PER VECCHI PROBLEMI: STIPSI E POLIETILENGLICOLE.
AUTHOR: Fontana M.; Martelli L.; Condo V.
CORPORATE SOURCE: M. Fontana, Unita Operativa di Pediatria, Ospedale dei Bambini Vittore Buzzi, Milano, Italy
SOURCE: Medico e Bambino, (31 Dec 2004) Vol. 23, No. 11, pp. 706-711. .
Refs: 35
ISSN: 1591-3090 CODEN: MBAMFC
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
039 Pharmacy
LANGUAGE: Italian
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 2005
Last Updated on STN: 24 Feb 2005
AB Drugs which are commonly used to soften the stools include mineral oils and osmotic laxatives. While the former are not recommended in paediatric patients, the latter, such as lactulose and lactitol, which are equivalent, must be given at significantly higher dosage than recommended by Italian manufacturers and their effect is at least partially due to modification of bacterial flora. Polyethylene glycols (PEG) are molecules of diverse weight which cannot be absorbed nor metabolized. PEG (either PEG 3350 or PEG 4000), at the concentration of 7.1 percent keeps the accompanying water in the intestine without any further drawing in of water from the intestinal wall, thus avoiding the risk of dehydration. High volumes of PEG can be used for complete intestinal lavage, as for colonoscopy, or for treating severe foecal impaction. Low volumes, on average 1 g/kg/die, i.e. 15 ml/kg/die solution to be increased or reduced depending on effect, are effective in the great majority of cases for treating chronic constipation. In PEG products manufactured in Italy salts give an unpleasant flavour which is not present in a product recently marketed in the US, which contains only pure PEG.

L18 ANSWER 6 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2005086809 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15716622
TITLE: Neostigmine for the treatment of acute hepatic encephalopathy with acute intestinal pseudo-obstruction in a cirrhotic patient.
AUTHOR: Park Chang Hwan; Joo Young Eun; Kim Hyun Soo; Choi Sung Kyu; Rew Jong Sun; Kim Sei Jong
CORPORATE SOURCE: Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea.

SOURCE: Journal of Korean medical science, (2005 Feb) Vol. 20, No. 1, pp. 150-2.
Journal code: 8703518. ISSN: 1011-8934.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 18 Feb 2005
Last Updated on STN: 12 Jul 2005
Entered Medline: 11 Jul 2005

AB We treated a 49-yr-old man with neostigmine, who had liver cirrhosis, acute hepatic encephalopathy, and acute intestinal pseudoobstruction. He was admitted in a state of hepatic confusion. On physical examination, the abdomen was distended; and bowel sound was absent. Plain abdomen film revealed multiple air-fluid levels and distention of bowel loops. Initially, we gave him lactulose enemas every 6 hr for one day without improvement in his mental state. Furthermore, he became to a state of coma. Therefore, we gave him 0.5 mg of neostigmine subcutaneously to improve his peristaltic movement, and 2 L of polyethylene glycol electrolyte solution through a nasogastric tube for 4 hr to reduce the production and absorption of gut-derived toxins of nitrogenous compounds. After these treatments, the venous ammonia level decreased to the normal range within 12 hr, and the coma disappeared after 2 days. We suggest that neostigmine may be one of the most effective treatments to initiate peristaltic movement and bowel cleansing in cirrhotic patients with acute hepatic encephalopathy and acute intestinal pseudoobstruction.

L18 ANSWER 7 OF 19 EMBASE
ACCESSION NUMBER: 95126813 EMBASE
DOCUMENT NUMBER: 1995126813
TITLE: Small intestinal absorption of polyethylene glycol 400 to 1,000 in the portacaval shunted rat.
AUTHOR: Pantzar N.; Bergqvist P.B.F.; Bugge M.; Olaison G.; Lundin S.; Jeppsson B.; Westrom B.; Bengtsson F.
CORPORATE SOURCE: Department of Clinical Pharmacology, Lund University Hospital,S-221 85 Lund, Sweden
SOURCE: Hepatology, (1995) Vol. 21, No. 4, pp. 1167-1173. .
ISSN: 0270-9139 CODEN: HPTLD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 1995
Last Updated on STN: 16 May 1995

AB Functional changes of the intestinal barrier that may occur after the creation of a portacaval shunt (PCS) were investigated. After chronic PCS in the rat, the intestinal absorption of and the jejunal permeability to the inert polymer marker polyethylene glycol (PEG) with molecular weight (Mw) ranging from 400 to 1,000 g/mol were investigated. The PEG mixture was orally fed to PCS and sham-operated rats, and urine was collected for 24 hours to obtain the urinary recovery of the different PEG polymers as a measure of intestinal absorption. To study the intestinal permeability, segments from the proximal small intestine were incubated in diffusion chambers with the PEG mixture on the mucosal side, and samples were withdrawn from the serosal side for analysis. The urinary recovery for the PEGs increased ($P < .01$) while the tissue permeability decreased ($P < .001$) in the PCS group rats in comparison with

Sham-operated rats. The increased absorption in vivo was caused neither by altered renal clearance, nor by changed portal blood pressure. The decreased jejunal permeability in the PCS rats could be explained by a reduction of the mucosal area by shortening of the microvilli. This discrepancy indicates that changes in permeability and absorption may not be parallel during PCS. It is possible that these changes also may be affected by nutritional factors, drug therapy, as well as toxic substances.

L18 ANSWER 8 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2003470541 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14532731
TITLE: A study for clinical correlation of neuropsychological test and brain magnetic resonance spectroscopy in patients with minimal hepatic encephalopathy.
AUTHOR: Nam Soon Woo; Kim Jin Il; Park Soo Heon; Han Nam Ik; Han Joon-Yeol; Ahn Byung Min; Kim Jae Kwang; Choi Sang Wook; Chung Kyu Won; Sun Hee Sik; Yang Dong Won; Ahn Kook Jin; Lee Jae Moon
CORPORATE SOURCE: Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea.
SOURCE: The Korean journal of gastroenterology = Taehan Sohwagi Hakhoe chi, (2003 Jul) Vol. 42, No. 1, pp. 50-6.
Journal code: 101189416. ISSN: 1598-9992.
PUB. COUNTRY: Korea
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Korean
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 9 Oct 2003
Last Updated on STN: 16 Apr 2004
Entered Medline: 15 Apr 2004

AB BACKGROUND/AIMS: The aim of the study was to correlate neuropsychological test results with regional cerebral biochemistry determined by magnetic resonance spectroscopy (MRS) in patients with minimal hepatic encephalopathy (MHE). METHODS: The patients with liver disease were divided into 4 groups; group 1 chronic hepatitis; group 2, liver cirrhosis (LC) without a history of HE; group 3, LC with a history of HE of no manifestation, and group 4, LC with overt HE. All patients were examined using neuropsychological tests and brain MRS. RESULTS: Trail making, Digit span, Digit symbol, and Peg board test in groups 2 and 3 were significantly different compared with control. These neuropsychological tests were regarded more available test for diagnosis of MHE. In the LC patients, compared with control, MRS results showed a typical pattern with decrease of myoinositol/Cr (0.24+/-0.24 vs. 0.68+/-0.10, $p<0.05$) and increased glutamine-glutamate/Cr (2.97+/-0.80 vs. 1.94+/-0.47, $p<0.05$). The difference of myoinositol/Cr and glutamine-glutamate/Cr between patients with MHE and control was statistically significant (0.16+/-0.15 vs. 0.68+/-0.10, 3.11+/-0.72 vs. 1.94+/-0.47, $p<0.05$). CONCLUSIONS: Neuropsychological tests and MRS maybe useful for diagnosing MHE.

L18 ANSWER 9 OF 19 MEDLINE on STN
ACCESSION NUMBER: 90014544 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2552270
TITLE: Cortical benzodiazepine receptor binding in a rabbit model of hepatic encephalopathy: the effect of Triton X-100 on receptor solubilization.
AUTHOR: Rossle M; Mullen K D; Jones E A
CORPORATE SOURCE: Liver Diseases Section, NIDDK, Bethesda, Maryland 20892.
SOURCE: Metabolic brain disease, (1989 Sep) Vol. 4, No. 3, pp. 203-12.
Journal code: 8610370. ISSN: 0885-7490.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198911
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 8 Nov 1989

AB Increased benzodiazepine (BZ) receptor density has been reported in brains of rabbits with hepatic encephalopathy (HE) due to galactosamine (GalN)-induced fulminant hepatic failure (FHF). These data were generated using detergent-Triton X-100-treated neural membranes. While performing further studies it was noted that the increase in BZ receptor density was not demonstrable when Triton X-100 preparation was not employed. Accordingly the binding of [3H] flunitrazepam, a BZ ligand, to neural membranes from cortices of normal rabbits and rabbits with HE due to (GalN)-induced FHF was studied with and without detergent preparation. Scatchard plot analysis of the binding data indicated that when no detergent was employed, the apparent affinity and density of BZ receptors were similar for control membranes and membranes from animals in HE. BZ receptors from animals in HE were shown to be more resistant to solubilization by Triton than control membranes. These findings (a) afford a potential explanation for the apparent increase in density of BZ receptors in this model when Triton treatment of neural membranes is utilized and (b) suggest that recent evidence for increased GABAergic tone in the syndrome of HE is not dependent on an increased density of BZ receptors.

L18 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1980:453919 CAPLUS
DOCUMENT NUMBER: 93:53919
TITLE: Development of a lavage solution associated with minimal water and electrolyte absorption or secretion
AUTHOR(S): Davis, Glenn R.; Ana, Carol A. Santa; Morawski, Stephen G.; Fordtran, John S.
CORPORATE SOURCE: Dep. Med., Baylor Univ. Med. Cent., Dallas, TX, 75246, USA
SOURCE: Gastroenterology (1980), 78(5, Pt. 1), 991-5
CODEN: GASTAB; ISSN: 0016-5085
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A solution for total gut perfusion which has min. H2O and electrolyte absorption or secretion used Na2SO4 as the predominant salt. The electrolyte concns. were (in mequiv/L): Na 125, SO4 80, Cl 35, HCO3 20, K 10. The solution also contained 80 mM poorly absorbed nonelectrolyte mannitol [69-65-8] or polyethylene glycol [25322-68-3]. The solns. are useful in colon cleansing, barium enema, prior to surgery, or therapeutically such as bowel cleaning in patients with hepatic encephalopathy or as a rapid washout for ingested toxins.

IT Isotonic solutions
(for gut perfusion, sodium sulfate in)
IT Intestine
(perfusion of, sodium sulfate electrolyte solns. for)
IT 7757-82-6, biological studies
RL: BIOL (Biological study)
(gut perfusion electrolyte solution containing)
IT 69-65-8 25322-68-3
RL: BIOL (Biological study)
(gut perfusion electrolyte solution containing sodium sulfate and)

L18 ANSWER 11 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95029742 EMBASE
DOCUMENT NUMBER: 1995029742
TITLE: [Use of polyethylene glycol 4000 for the treatment of posthemorrhagic encephalopathy [1]]. UTILISATION DU POLYETHYLENE GLYCOL 4000 DANS L'ENCEPHALOPATHIE HEPATIQUE LIEE AUX HEMORRAGIES DIGESTIVES [1].
AUTHOR: Roblin X.; Blais J.; Legrand C.; Andre F.; Pothin A.
CORPORATE SOURCE: Service d'Hepato-Gastroenterologie, CHD Flix-Guyon,F-97405 Saint-Denis de la Reunion, France
SOURCE: Gastroenterologie Clinique et Biologique, (1994) Vol. 18, No. 12, pp. 1146. .
ISSN: 0399-8320 CODEN: GCBIDC
COUNTRY: France
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 006 Internal Medicine
008 Neurology and Neurosurgery
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: French
ENTRY DATE: Entered STN: 22 Feb 1995
Last Updated on STN: 22 Feb 1995
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L18 ANSWER 12 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:311325 BIOSIS
DOCUMENT NUMBER: PREV199598325625
TITLE: Use of polyethylene glycol 4000 for the treatment of posthemorrhagic encephalopathy.
AUTHOR(S): Roblin, Xavier; Blais, Jacques; Legrand, Christope; Andre, Francois; Pothin, Agnes
CORPORATE SOURCE: Serv. Hepato-Gastroenterol., CHD Felix-Guyon, F-97405 Saint-Denis, La Reunion, France
SOURCE: Gastroenterologie Clinique et Biologique, (1994) Vol. 18, No. 12, pp. 1146.
CODEN: GCBIDC. ISSN: 0399-8320.
DOCUMENT TYPE: Letter
LANGUAGE: French
ENTRY DATE: Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995
IT Major Concepts
Behavior; Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Nervous System (Neural Coordination); Pharmacology; Psychiatry (Human Medicine, Medical Sciences); Toxicology
IT Chemicals & Biochemicals
POLYETHYLENE GLYCOL 4000; MANNITOL; LACTULOSE; ALCOHOL
IT Miscellaneous Descriptors
ALCOHOL CONSUMPTION; BLAKEMORE TUBE; CASE STUDY; CIRRHOSIS; GASTROINTESTINAL HEMORRHAGE; HEPATIC ENCEPHALOPATHY ; LACTULOSE; MANNITOL; POLYETHYLENE GLYCOL 4000
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 69-65-8Q (MANNITOL)

87-78-5Q (MANNITOL)
4618-18-2 (LACTULOSE)
64-17-5 (ALCOHOL)
25322-68-3 (POLYETHYLENE GLYCOL 4000)

L18 ANSWER 13 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:317826 BIOSIS
DOCUMENT NUMBER: PREV199598332126
TITLE: Is the treatment of acute hepatic encephalopathy justified in cirrhosis?.
AUTHOR(S): Doffoel, Michel [Reprint author]; Vetter, Denis
CORPORATE SOURCE: Serv. Hepato-Gastroenterol., Hopital Civil, F-67091 Strasbourg Cedex, France
SOURCE: Gastroenterologie Clinique et Biologique, (1994) Vol. 18, No. 12, pp. 1055-1056.
CODEN: GCBIDC. ISSN: 0399-8320.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: French
ENTRY DATE: Entered STN: 30 Jul 1995
Last Updated on STN: 30 Jul 1995
IT Major Concepts
Behavior; Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Digestive System (Ingestion and Assimilation); Infection; Mathematical Biology (Computational Biology); Metabolism; Nervous System (Neural Coordination); Pharmacology; Psychiatry (Human Medicine, Medical Sciences); Toxicology
IT Chemicals & Biochemicals
LACTULOSE; NEOMYCIN; BENZODIAZEPINE; MANNITOL; POLYETHYLENE GLYCOL
IT Miscellaneous Descriptors
ANASTOMOSIS; ANTIBIOTIC THERAPY; BACTERIAL INFECTION; BENZODIAZEPINE; DIGESTIVE HEMORRHAGE; DISACCHARIDE; ETIOLOGY; HEPATOCELLULAR INSUFFICIENCY; HYDROELECTROLYTIC DISORDER; LACTULOSE; MANNITOL; NEOMYCIN; NEUROPSYCHIATRIC MANIFESTATION; POLYETHYLENE GLYCOL; STATISTICAL ANALYSIS; TOXICITY
ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN 4618-18-2 (LACTULOSE)
1404-04-2 (NEOMYCIN)
12794-10-4 (BENZODIAZEPINE)
69-65-8Q (MANNITOL)
87-78-5Q (MANNITOL)
25322-68-3 (POLYETHYLENE GLYCOL)

L18 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:408669 CAPLUS
DOCUMENT NUMBER: 145:50903
TITLE: Pharmaceutical compositions containing safflower yellow a, and its preparation
INVENTOR(S): Zhang, Yumei
PATENT ASSIGNEE(S): Albela Pharmaceutical Holding (Tonghua) Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 17 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent

LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1762342	A	20060426	CN 2005-10109599	20051028
PRIORITY APPLN. INFO.:			CN 2005-10109599	20051028

AB The pharmaceutical composition consists of aceglutamide and safflower yellow A, and at weight of aceglutamide is 10-500 fold of safflower yellow. The safflower yellow is prepared by adding water or 5-95% ethanol or 5-95% acetone solvent or the the mixture of them to the medicinal materials of Carthamus tinctorius, extracting, combining the extracted solution, adding 10-70% acetone, 0.05-5% crystallization assistant, storing for 12-70 h, and crystallizing to obtain safflower yellow. The crystallization assistant is selected from organic bases or alkaloids such as triethanolamine, aconitine, uncarine, ligustrazine, caffeine, matrine, kopsine, ecboline, etc.; or salts such as sodium citrate, sodium acetate, sodium bicarbonate, sodium oxalate, etc. The safflower yellow A is prepared by dissolving safflower yellow with water, or separating with macroporous resin treated by 0.1-15 ethanol, eluting with ethanol, collecting, combining eluent of 30 and 45% ethanol, and reduced pressure drying to obtain safflower yellow A. The patent relates to the application of the pharmaceutical composition to prepare the medicine for treating occlusive cerebrovascular disease, hepatic coma , hemiplegia, coronary disease, vasculitis, depression, etc.

IT Drug delivery systems
(capsules; pharmaceutical composition containing safflower yellow A)

IT Drug delivery systems
(granules; pharmaceutical composition containing safflower yellow A)

IT Drug delivery systems
(injections; pharmaceutical composition containing safflower yellow A)

IT Carthamus tinctorius
(pharmaceutical composition containing safflower yellow A)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing safflower yellow A)

IT Drug delivery systems
(tablets; pharmaceutical composition containing safflower yellow A)

IT 1401-20-3, Safflower yellow 2490-97-3, Aceglutamide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing safflower yellow A)

IT 58-08-2, Caffeine, biological studies 62-76-0, Sodium oxalate 68-04-2, Sodium citrate 69-65-8, Mannite 102-71-6, Triethanolamine, biological studies 127-09-3, Sodium acetate 144-55-8, Sodium bicarbonate, biological studies 302-27-2, Aconitine 519-02-8, Matrine 557-04-0, Magnesium stearate 559-48-8, Kopsine 1124-11-4, Ligustrazine 1310-73-2, Sodium hydroxide, biological studies 7631-86-9, Silicon dioxide, biological studies 8006-25-5, Ecboline 9003-39-8, Polyvinylpyrrolidone 9004-54-0, Dextran, biological studies 9005-25-8, Starch, biological studies 9063-38-1, Sodium carboxymethyl starch 25322-68-3, Polyethylene glycol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing safflower yellow A)

L18 ANSWER 15 OF 19 MEDLINE on STN
ACCESSION NUMBER: 90246063 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2336497
TITLE: [Is the prognosis of patients with variceal hemorrhage

determined by the severity of the underlying disease?]. Ist die Prognose der Patienten mit Varizenblutung durch den Schweregrad der Grundkrankheit determiniert?.
AUTHOR: Eigenmann F; Neff A; van den Brandt-Gradel V; Halter F
CORPORATE SOURCE: Gastroenterologische Abteilung des Inselspitals Bern.
SOURCE: Schweizerische Rundschau fur Medizin Praxis = Revue suisse de medecine Praxis, (1990 Apr 10) Vol. 79, No. 15, pp. 455-7.
Journal code: 8403202. ISSN: 1013-2058.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199006
ENTRY DATE: Entered STN: 6 Jul 1990
Last Updated on STN: 6 Jul 1990
Entered Medline: 8 Jun 1990

AB This retrospective analysis includes all patients in whom endoscopic sclerotherapy was initiated because of bleeding oesophageal varices during the years 1984 to 1986. Of the total of 107 patients (77 men, 30 women, mean age 56 years) a majority of 71 (66.3%) had alcoholic liver disease as the underlying cause of portal hypertension. Varices were injected with ethoxysclerol 1% in weekly sessions if possible until they were completely eradicated. Initially 27 patients (25.2%) were classified as Child's class A, 52 (48.5%) as Child's class B and 27 as Child's class C. At the time of analysis 46 patients (42.9%) had died. 17 patients died of uncontrolled variceal haemorrhage one of them after a completed course of sclerotherapy, 15 died in hepatic coma. The cumulative survival rate after one year was 63.8% overall, 84.7% for patients in Child's class A, 75.4% for patients in Child's class B and 21.3% for patients in Child's class C. The one year survival rate for the 50 patients who failed to complete a course of sclerotherapy was 26.9%. The one year survival rate for alcoholics as a group (63%) was the same as for non-alcoholics (64.2%). 40 patients had non-fatal episodes of bleeding, 15 of whom bled after completion of a course of endoscopic sclerotherapy (median delay 174 days after completion of sclerotherapy). We conclude from our results that the outcome after sclerotherapy for oesophageal varices is determined mainly by the severity of the underlying liver disease.(ABSTRACT TRUNCATED AT 250 WORDS)

L18 ANSWER 16 OF 19 MEDLINE on STN
ACCESSION NUMBER: 87010638 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3760866
TITLE: Brain alpha-ketoglutarate dehydrogenase complex: kinetic properties, regional distribution, and effects of inhibitors.
AUTHOR: Lai J C; Cooper A J
CONTRACT NUMBER: AM 16739 (NIADDK)
SOURCE: Journal of neurochemistry, (1986 Nov) Vol. 47, No. 5, pp. 1376-86.
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198611
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 19 Nov 1986

AB The substrate and cofactor requirements and some kinetic properties of the alpha-ketoglutarate dehydrogenase complex (KGDHC; EC 1.2.4.2, EC 2.3.1.61, and EC 1.6.4.3) in purified rat brain mitochondria were studied. Brain mitochondrial KGDHC showed absolute requirement for alpha-ketoglutarate,

CoA and NAD, and only partial requirement for added thiamine pyrophosphate, but no requirement for Mg2+ under the assay conditions employed in this study. The pH optimum was between 7.2 and 7.4, but, at pH values below 7.0 or above 7.8, KGDHC activity decreased markedly. KGDHC activity in various brain regions followed the rank order: cerebral cortex greater than cerebellum greater than or equal to midbrain greater than striatum = hippocampus greater than hypothalamus greater than pons and medulla greater than olfactory bulb. Significant inhibition of brain mitochondrial KGDHC was noted at pathological concentrations of ammonia (0.2-2 mM). However, the purified bovine heart KGDHC and KGDHC activity in isolated rat heart mitochondria were much less sensitive to inhibition. At 5 mM both beta-methylene-D,L-aspartate and D,L-vinylglycine (inhibitors of cerebral glucose oxidation) inhibited the purified heart but not the brain mitochondrial enzyme complex. At approximately 10 microM, calcium slightly stimulated (by 10-15%) the brain mitochondrial KGDHC. At concentrations above 100 microM, calcium (IC50 = 1 mM) inhibited both brain mitochondrial and purified heart KGDHC. The present results suggest that some of the kinetic properties of the rat brain mitochondrial KGDHC differ from those of the purified bovine heart and rat heart mitochondrial enzyme complexes. They also suggest that the inhibition of KGDHC by ammonia and the consequent effect on the citric acid cycle fluxes may be of pathophysiological and/or pathogenetic importance in hyperammonemia and in diseases (e.g., hepatic encephalopathy, inborn errors of urea metabolism, Reye's syndrome) where hyperammonemia is a consistent feature. Brain accumulation of calcium occurs in a number of pathological conditions. Therefore, it is possible that such a calcium accumulation may have a deleterious effect on KGDHC activity.

L18 ANSWER 17 OF 19 EMBASE

ACCESSION NUMBER: 2005325990 EMBASE

TITLE: Pegylated-interferon alpha 2b and ribavirin for recurrent hepatities C after liver liver transplantation: From a Canadian experience to recommendations for therapy.

AUTHOR: Babatin M.; Schindel L.; Burak K.W.

CORPORATE SOURCE: Dr. K.W. Burak, Health Science Centre, 3350 Hospital Drive Northwest, Calgary, Alta. T2N 4N1, Canada. kwburak@ucalgary.ca

SOURCE: Canadian Journal of Gastroenterology, (2005) Vol. 19, No. 6, pp. 359-365. .
Refs: 24
ISSN: 0835-7900 CODEN: CJGAEJ

COUNTRY: Canada

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English; French

ENTRY DATE: Entered STN: 1 Sep 2005
Last Updated on STN: 1 Sep 2005

AB Background: Recurrent hepatitis C (HCV) after liver transplantation (LT) is often more aggressive and treatments tend to be less successful. Pegylated-interferon and ribavirin are the standard of care for the treatment of HCV; however, there is limited published experience of its use after LT. Objective: To report the results of pegylated-interferon alpha 2b (PEG-IFN) plus ribavirin for the treatment of recurrent HCV after LT and compare the results with published data. Methods: Thirteen patients with recurrent HCV were treated with PEG-IFN plus ribavirin. Liver biopsies demonstrated early-stage disease in eight patients and advanced fibrosis in five patients. The average starting

dose of PEG-IFN was 0.91 μg/kg (range 0.5 μg/kg to 1.1 μg/kg) per week and ribavirin was started at 662 mg (range 0 mg to 1200 mg) per day. PEG-IFN treatment began an average of 24 months after LT (range six to 73 months). The dose of PEG-IFN was increased in four patients but only two reached 1.5 μg/kg. The ribavirin dose was increased in four, reduced in six and only seven patients reached a ribavirin dose greater than 10.6 mg/kg. Results: A sustained virological response was seen in four of 13 (30.7%) patients and in four of eight (50%) patients with early-stage disease compared with zero of five patients with advanced fibrosis (P=0.1). Cytopenias were common and therapy was poorly tolerated in four of five patients with advanced fibrosis, including acute cellular rejection in three, renal failure in two, liver decompensation in four and death in three. Conclusions: Although a reasonable sustained virological response can be achieved with the use of PEG-IFN and ribavirin, the treatment is very poorly tolerated by patients with advanced-stage recurrent HCV. Treatment should be instituted before the development of significant fibrosis after LT.

L18 ANSWER 18 OF 19 EMBASE

ACCESSION NUMBER: 2004438254 EMBASE

TITLE: [Coinfection HIV-HCV: Which therapeutic strategy is recommended?].
COINFECTION VIH-VHC: QUELLE PRISE EN CHARGE?.

AUTHOR: Aumaitre H.; Chauvet E.; Medus M.; Saada M.
CORPORATE SOURCE: H. Aumaitre, Serv. des Maladies Infect. et Trop., Centre Hospitalier Saint Jean, 66046 Perpignan, France. hugues.aumaitre@ch-perpignan.fr

SOURCE: Antibiotiques, (2004) Vol. 6, No. 3, pp. 151-163. .
Refs: 71
ISSN: 1294-5501 CODEN: ANTBFQ
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: French
SUMMARY LANGUAGE: French; English
ENTRY DATE: Entered STN: 28 Oct 2004
Last Updated on STN: 28 Oct 2004

AB Since the introduction of antiretroviral therapies in HIV patients, associated HCV infection has become the most important factor for therapeutic uses and for death rates. This evolution imposes the analysis of the serologic HCV status in all HIV positive patients. Besides serology tests, ARN dosage and determination of the genotype have become the bases of virologic status. It is only by means of liver biopsy and its pathology analysis that the evaluation of fibrosis degree and the decision for treatment can be established. The evaluation of the degree of severity of the hepatitis must also be based on biochemical tests and on the echography. Diverse factors of co-morbidity must be taken into account (alcoholism, hepatic steatosis, drug addictions) for the therapeutic decision. The duration of therapy is defined after several consecutive consultations showing that there is no major contra-indication, that the HIV treatment can be considered stable, and after having informed the patient on the objectives of the treatment, on its potential side effects for one year treatment. The combination PEG-interferon + ribavirin must be strictly controlled and adjusted as a function of tolerance. Monthly followed consultations permit patient training, and are in favour of successful treatment.

Virologic curing is expected in 25 to 35% patients but non-responders must be seen regularly. Chronic treatments and new antiproteases are under evaluation. Cirrhotic patients (treated or not) should be seen at least once every 3 months and in case of the development of tumour or hepatic total failure they must be transferred to surgery teams. .COPYRGT. Masson, Paris, 2003.

L18 ANSWER 19 OF 19 MEDLINE on STN

ACCESSION NUMBER: 2005577603 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16255295
TITLE: [Liver cirrhosis in adults: etiology and specific treatments].
Etiologies des cirrhoses et specificites de leur traitement.
AUTHOR: Fartoux Laetitia; Serfaty Lawrence
CORPORATE SOURCE: Service d'hepatologie, hopital Saint-Antoine, 75571 Paris.. laetitia.fartoux@sat.ap-hop.paris.fr
SOURCE: La Revue du praticien, (2005 Sep 30) Vol. 55, No. 14, pp. 1539-48.
Journal code: 0404334. ISSN: 0035-2640.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: French
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 1 Nov 2005
Last Updated on STN: 16 Dec 2005
Entered Medline: 2 Dec 2005

AB Cirrhosis is the result of chronic inflammation and of the progressive increase of fibrosis. In France, hepatitis C infection is the second cause of cirrhosis after alcohol abuse. The other causes of cirrhosis are: hepatitis B infection, genetic haemochromatosis, autoimmune hepatitis, primary biliary cirrhosis, drug-induced cirrhosis, secondary biliary cirrhosis, Wilson's disease and al-antitrypsin deficiency. Etiological treatment is based upon: abstinence in case of alcoholic cirrhosis, the combination of pegylated interferon alpha (PEG IFN) with ribavirin in case of C viral cirrhosis, the PEG IFN and the nucleoside analogs in case of B viral cause; corticosteroids and immunosuppressive drugs in case of autoimmune cirrhosis; venesections in case of genetic haemochromatosis and stopping the drug in case of drug-induced cirrhosis. The complications of cirrhosis such as ascites, oesophageal varices, bleeding, hepatic encephalopathy and hepatocellular carcinoma mainly explain the high rate of morbidity and mortality. Liver transplantation is the established therapy for decompensated liver disease of any etiology significantly changed the outcome of patients with advanced cirrhosis.

=>

Alimentary Pharmacology & Therapeutics

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Colon cleansing preparation for gastrointestinal procedures.

Review Article

Alimentary Pharmacology & Therapeutics. 15(5):605-611, May 2001.

Toledo, T. K.; Dipalma, J. A. *

Abstract:

Adequate cleansing is essential for reliable diagnostic and surgical colon procedures. Accu good preparation. Patient compliance is enhanced by simplicity and well-tolerated methods

Several methods are available. Diet and cathartic regimens utilize clear liquids or diets desi colonic residue. Laxatives, cathartics and enemas are employed. Gut lavage solutions are electrolyte lavage products. Oral sodium phosphate solutions and tablets are available and good efficacy with a small volume of administration.

For colonoscopy and colon surgery preparation, these methods have been proven safe and X-ray, lavage requires an adjunctive agent such as bisacodyl to enhance barium coating. O tolerated.

This review discusses the development and clinical experience with various colon cleansing

LIPPINCOTT WILLIAMS & WILKINS
J·P·G·N JOURNAL OF PEDIATRIC GASTROENTEROLOGY AND NUTRITION

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Hammer HF; Santa Ana CA; Schiller LR; Fordtran JS.
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Department of Internal Medicine, Baylor University of Medical Center, Dallas, Texas 75246.
Title
Studies of osmotic diarrhea induced in normal subjects by ingestion of polyethylene glycol and lactulose.
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Diarrhea/et [Etiology]
*Diarrhea/pp [Physiopathology]
*Disaccharides/ae [Adverse Effects]
Electrolytes/an [Analysis]
Feces/an [Analysis]
Humans
Intestinal Absorption/de [Drug Effects]
*Lactulose/ae [Adverse Effects]
Male
Osmolar Concentration
*Polyethylene Glycols/ae [Adverse Effects]
Reference Values
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Water/an [Analysis]
Abstract
The purpose of these studies was to gain insight into the pathophysiology of pure osmotic diarrhea and the osmotic diarrhea caused by carbohydrate malabsorption. Diarrhea was induced in normal volunteers by ingestion of polyethylene glycol (PEG), which is nonabsorbable, not metabolized by colonic bacteria, and carries no electrical charge. In PEG-induced diarrhea, (a) stool weight was directly correlated with the

total mass of PEG ingested; (b) PEG contributed 40-60% of the osmolality of the fecal fluid, the remainder being contributed by other solutes either of dietary, endogenous, or bacterial origin; and (c) fecal sodium, potassium, and chloride were avidly conserved by the intestine, in spite of stool water losses exceeding 1,200 g/d. Diarrhea was also induced in normal subjects by ingestion of lactulose, a disaccharide that is not absorbed by the small intestine but is metabolized by colonic bacteria. In lactulose-induced diarrhea, (a) a maximum of approximate 80 g/d of lactulose was metabolized by colonic bacteria to noncarbohydrate moieties such as organic acids; (b) the organic acids were partially absorbed in the colon; (c) unabsorbed organic acids obligated the accumulation of inorganic cations (Na greater than Ca greater than K greater than Mg) in the diarrheal fluid; (d) diarrhea associated with low doses of lactulose was mainly due to unabsorbed organic acids and associated cations, whereas with larger doses of lactulose unmetabolized carbohydrates also played a major role; and (e) the net effect of bacterial metabolism of lactulose and partial absorption of organic acids on stool water output was done dependent. With low or moderate doses of lactulose, stool water losses were reduced by as much as 600 g/d (compared with equimolar osmotic loads of PEG); with large dose, the increment in osmotically active solutes within the lumen exceeded the increment of the ingested osmotic load, and the severity of diarrhea was augmented.

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ARTICLE LINKS:
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Journal of Pediatric Gastroenterology and Nutrition: Volume 35(5) November 2002 pp 707-708

Author's Reply to Dr. Geraint [Letters to the Editor]

Loening-Baucke, Vera

Department of Pediatrics University

of Iowa Hospital and Clinics

Iowa City, IA, U.S.A.

To the Editor:

We stated in our recent publication (1) that polyethylene glycol electrolyte solution (PEG-ELS) when taken in low volumes daily was effective, safe, well-tolerated, and devoid of significant side effects in the short-term (2) and long-term treatment (3) of constipation in adults. No net absorption or secretion was presumed for the use of smaller volumes, but recent work has shown that low-volume administration resulted in nearly complete absorption of the salt component of the solution, which could potentially lead to dangerous sequelae, especially for patients with renal impairment or congestive heart disease (4,5).

The daily sodium load from PEG-ELS was about 1 g, when given as a daily dose of 500 ml PEG-ELS (containing 29.5 g PEG 3350) by Corazziari et al. (3). They observed no change in serum electrolytes after six months in otherwise healthy constipated adults. In another study, 60 g of PEG without electrolytes improved the constipation in patients with slow transit constipation (6). Some of our chronically constipated and encopretic children required 68 g of PEG without electrolytes per day. This amount of PEG would be contained in 5 sachets of macrogol 3350 (Movicol®, Norgine Limited, Oxbridge, Middlesex, UK) with 1.8 g of sodium chloride and 0.9 g of sodium hydrogen carbonate, containing 0.94 g of sodium. This amount represents a significant fraction of the daily sodium allowance for patients requiring a sodium-restricted diet of 2 or 3 g/d. We must agree with Dr. Geraint, that the amount of sodium chloride and sodium bicarbonate contained in PEG-ELS is marked and should be calculated into their daily allowance by patients who must observe a sodium-restricted diet.

With regard to the electrolyte disturbance (particularly hypokalemia) that can be induced by the use of laxatives as mentioned by Dr. Geraint, we just concluded a study on the long-term safety and efficacy of PEG 3350 without electrolytes in constipated children, 2 to 17 years of age (7). No abnormality in serum electrolytes was observed after daily use of PEG without electrolytes for 3 to 30 months.

In summary, using PEG-ELS for daily treatment of constipation adds a significant fraction to the sodium allowance of patients requiring a sodium-restricted diet. No harmful loss of electrolytes was observed in our chronically constipated children receiving PEG without electrolytes for up to 30 months.

Vera Loening-Baucke

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[Fulltext Link] [CrossRef] [Context Link]

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[Medline Link] [Context Link]

3. Corazziari E, Badiali D. Bazzocchi G, et al. Long term efficacy, safety, and tolerability of low daily doses of isosmotic polyethylene glycol electrolyte balanced solution (PMF-100) in the treatment of functional chronic constipation. Gut 2000; 46:522-6.
[Fulltext Link] [CrossRef] [Context Link]

4. Hammer HF, Santa Ana CA, Schiller LR, Fordtran JS. Studies of osmotic diarrhea induced in normal subjects by ingestion of polyethylene glycol and lactulose. J Clin Invest 1989; 84:1056-62.
[Medline Link] [Context Link]

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[CrossRef] [Context Link]

6. Klauser AG, Muehldorfer BE, Voderholzer WA, Wenzel G, Mueller-Lissner SA. Polyethylene glycol 4000 for slow transit constipation. Z Gastroenterol 1995; 33:5-8.
[Context Link]

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[Context Link]

L9 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1975:475069 CAPLUS

DOCUMENT NUMBER: 83:75069

TITLE: Investigation of small bowel transit time in man utilizing pulmonary hydrogen (H2) measurements

AUTHOR(S): Bond, John H., Jr.; Levitt, Michael D.; Prentiss, Robin

CORPORATE SOURCE: Dep. Med., VA Hosp., Minneapolis, MN, USA

SOURCE: Journal of Laboratory and Clinical Medicine (1975), 85(4), 546-55
CODEN: JLCMAK; ISSN: 0022-2143

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pulmonary H2 excretion was used to quantitate the small bowel transit time in man. This technique was based on the observation that H2 was produced when carbohydrate was fermented by colonic bacteria and that this H2 production was reflected by a concomitant increase in breath H2. The time between ingestion of the unabsorbable disaccharide lactulose and the rise in breath H2 represented the small intestinal transit time of the head of the lactulose load as it passed through the gut. Following ingestion of a mixt. of polyethylene glycol (PEG) and lactulose by 9 subjects, transit time measured by H2 excretion correlated closely with the simultaneously determined time for PEG to reach the distal ileum. The ileal appearance of PEG preceded the rise in H2 excretion by a mean of 7.6 min. Transit time of 10 g of lactulose in 40 healthy subjects averaged 72 min. Repeated studies in 6 subjects showed good individual reproducibility with subsequent measurements differing from initial by a mean of ±14%. There was an inverse relation between transit time and dose of lactulose ingested by 9 subjects with 5, 10, and 20 g lactulose having mean transit times of 128, 94, and 40 min, resp. This technique appears to provide a simple, safe, and noninvasive means of studying small bowel transit time in man.

L9 ANSWER 6 OF 25 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 94246436 EMBASE
DOCUMENT NUMBER: 1994246436
TITLE: A study of colon preparation method for colonoscopy by using 500 ml of polyethylene glycol electrolyte lavage solution.
AUTHOR: Kanamori T.; Yokoyama Y.; Itoh M.; Takeuchi T.
CORPORATE SOURCE: I Department of Internal Medicine, Nagoya City University Med. School,Nagoya, Japan
SOURCE: Therapeutic Research, (1994) Vol. 15, No. SUPPL. 2, pp. 186-191. .
ISSN: 0289-8020 CODEN: THREEL
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 048 Gastroenterology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Sep 1994
Last Updated on STN: 14 Sep 1994

AB We have already reported the superiority of a colon preparation method (combined method) using polyethylene glycol electrolyte lavage solution (PEG-ELS) together with other laxatives to a method using only PEG-ELS. Of combined methods, the method using sodium picosulfate (10 ml) lactulose (90 ml), and PEG-ELS (1000 ml) has been excellent because of its high colon cleansing effect and good tolerance of patients. However, most patients have complained the distress of taking 1000 ml of PEG-ELS. Therefore we studied the usefulness of a new preparation method for colonoscopy by using 500 ml of PEG -ELS in terms of colon cleansing and patient acceptance. In this new method, 24 mg of sennoside was taken two days before examination, 10 ml of sodium picosulfate the day before, and 90 ml of lactulose and 500 ml of PEG-ELS on the day. In addition, the meals of the day before were restricted to bread or noodle, or other low residue diets. In colon cleansing effect, this new method has the same effect as our former method, i.e. about 171 (90.5%) of 189 cases were recognized as good colon cleansing effect. In patient tolerance, sixty (90.9%) of 66 patients who have experienced both methods within a year preferred to this new method. In conclusion, we appreciated that this is one of the best preparation methods for colonoscopy in terms of colon cleansing effect and patient tolerance.

ingentaconnect

Effects of lactulose and polyethylene glycol on colonic transit

Authors: Fritz, E.[1]; Hammer, H. F.[2]; Lipp, R. W.[2]; Högenauer, C.[2]; Stauber, R.[2]; Hammer, J.[1]

Source: Alimentary Pharmacology & Therapeutics, Volume 21, Number 3, February 2005, pp. 259-268(10)

Publisher: Blackwell Publishing

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Abstract:

Summary Background

: The effects of lactulose and polyethylene glycol on colonic transit are poorly established. Aim:

To assess the effects of these laxatives on colonic transit in normal subjects. Methods

: Colonic transit (mean residence time, cumulative counts in stool, counts remaining in the proximal or distal colon) was measured scintigraphically in normal subjects on the second and third day of a 3-day ingestion of 67–134 g/day lactulose, or 59 g/day polyethylene glycol. Results

: At similar stool weight (lactulose: 653 ± 120 g/day; polyethylene glycol: 522 ± 66 g/day), transit was significantly slower during 99 g/day lactulose when compared with 59 g/day polyethylene glycol; this was most pronounced in the distal colon (mean residence time: lactulose – 403 ± 55 min; polyethylene glycol – 160 ± 41.9 min). Short chain fatty acid concentration in 24-h stool correlated significantly with counts remaining in the distal colon at 12 h(r = 0.79, P = 0.001). Increasing lactulose doses were significantly associated with increasing stool weight (r = 0.79) and shorter mean residence time in the total (r = −0.56) and distal colon (r = −0.64). The sum of faecal carbohydrates plus short chain fatty acids was associated with stool weight (r = 0.95, P < 0.001). Conclusion

: Lactulose accelerates colonic transit. However, compared with polyethylene glycol, transit during lactulose is prolonged.

Document Type: Research article

DOI: 10.1111/j.1365-2036.2005.02244.x

Affiliations: 1: Universitätsklinik für Innere Medizin IV, Vienna **2:** Department of Internal Medicine, University of Graz, Graz, Austria

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Gastrointestinal Drugs

Laxatives

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Brand/Generic Name (Generics in italics)	Dosage/Strength	Status	Restrictions	Notes	Cost Sharing
Cephulac ***Lactulose*** *Encephalopathy*	Syrup - 10gm/15ml	NF			N/A
Colyte G *PEG 3350-KCl-NaBcb-NaCl-NaSulf*	Recon Soln -	NF			N/A
Duphalac ***Lactulose***	Solution - 10gm/15ml	NF			N/A
Enulose G ***Lactulose*** *Encephalopathy*	Solution - 10gm/15ml	✓			Tier 1
Fiber G *Fiber*	-	NF			N/A
FIBER DIET *Fiber*	-	NF			N/A
Fiber/C/Extra Calcium *Fiber-Vit C-Calcium*	-	NF			N/A
Generlac G ***Lactulose*** *Encephalopathy*	Solution - 10gm/15ml	✓			Tier 1
GlycoLax G ***Polyethylene Glycol*** *3350*	Powder -	✓			Tier 1
GlycoLax G ***Polyethylene Glycol*** *3350*	Powder Packet -	✓			Tier 1
Golytely G *PEG 3350-KCl-NaBcb-*	Recon Soln -	✓			Tier 2

NaCl-NaSulf				
HalfLytely Bowel Prep *Bisacodyl-PEG-KCl-NaBicar-NaCl*	-	✓		Tier 3
Kristalose ***Lactulose***	Powder Packet - 10gm	✓		Tier 3
Kristalose ***Lactulose***	Powder Packet - 20gm	✓		Tier 3
Lactulose G ***Lactulose***	Solution - 10gm/15ml	✓		Tier 1
MiraLax G ***Polyethylene Glycol*** *3350*	Powder -	NF		N/A
Nulytely G *PEG 3350-KCl-Na Bicarb-NaCl*	Recon Soln -	✓		Tier 2
PEG 3350 G ***Polyethylene Glycol*** *3350*	Recon Soln -	✓		Tier 1
Polyethylene Glycol 3350 G ***Polyethylene Glycol*** *3350*	Powder -	✓		Tier 1
Polyethylene Glycol 3350 G ***Polyethylene Glycol*** *3350*	Powder Packet -	✓		Tier 1
TriLyte G *PEG 3350-KCl-Na Bicarb-NaCl*	Recon Soln -	✓		Tier 1
Visicol *Sod Phos Mono-Sod Phos Dibasic*	Tab - 0.398-1.102gm	✓		Tier 3

Key for Product(s) Listed Above

✓ Formulary | NF Non-Formulary | PA Prior Authorization | NF Not Reimbursed

QL Quantity Limit | G Generic Available | ST Step Therapy | Notes

Managing Constipation in Adults: Patient Counseling and Triage

John Horn, PharmD, FCCP
Department of Pharmacy University of Washington
Seattle, Washington

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Release Date: January 1, 2006 **Expiration Date:** January 31, 2008

Faculty: ***John Horn, PharmD, FCCP***
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Disclosure Statements:
Dr. Horn is a speaker for Ortho-McNeil, Pfizer, Novartis, and Bristol-Myers Squibb.

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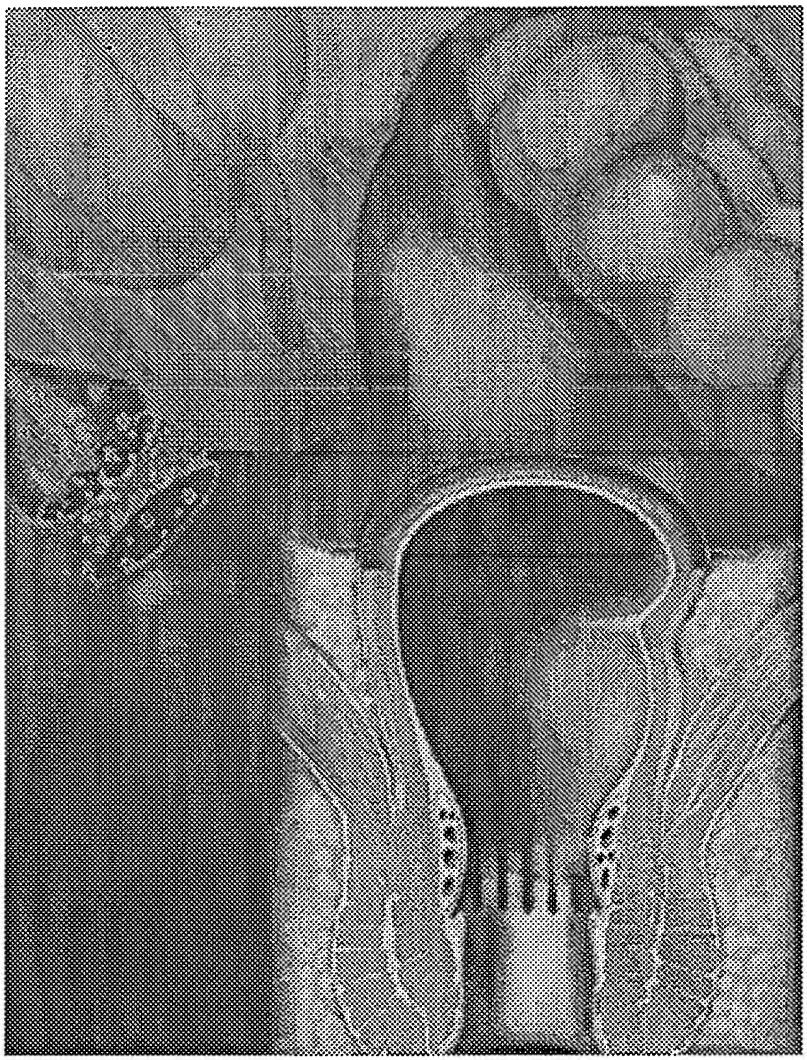
Program Number: 430-000-05-116-H01
Credits: 2.0 hours (0.2 CEUs)

Goal:
To educate pharmacists about the socioeconomic burden constipation imposes on patients and society, the place of traditional and novel therapeutic options for constipation, and the pharmacist's role in the assessment, triage, and care of adult patients with constipation.

Objectives:
After reading this article, the pharmacist should be able to:

- **Discuss** the epidemiology of constipation and the negative impact this disorder has on patients' daily lives, work productivity, and health care costs.
- **List** examples of primary and secondary causes of constipation and discuss the key questions to ask patients when determining the appropriateness of self-care or the need for referral to a physician.
- **Explain** the place in therapy of traditional treatment approaches for constipation, and compare and contrast efficacy and tolerability profiles of laxatives.
- **Discuss** the role of serotonin in GI tract function, and explain the place in therapy for serotonergic agents and emerging treatment options for patients with constipation.
- **Discuss** how pharmacists can help optimize the management of patients with constipation.

One of the most common gastrointestinal (GI) problems reported during physician visits,[1] constipation is a highly prevalent disorder that inflicts a heavy burden on patients, health care providers, and society at large. For many people, this condition is an occasional annoyance that can be successfully self-treated; for others, however, symptoms are chronic, highly bothersome, negatively affect their ability to lead productive lives, and result in frequent use of the health care system. Although constipation is common, potential causes are numerous, presenting a challenge for pharmacists responding to patients' requests for help in self-treatment. Understanding the key questions to ask is critical to pharmacists' ability to recommend appropriate treatments and, when necessary, refer for further evaluation. This article provides an overview of the epidemiology and socioeconomic burden of this disorder and the various treatment options (traditional, novel, emerging), and it offers strategies pharmacists can use to triage patients.



The colon has both internal and external muscles. Constipation can occur when the colon absorbs too much water or its muscle contractions are slow or sluggish.

Definition

Surprisingly, constipation has no formal definition, and physicians' and patients' perspectives of it vary. Whereas the definition used by physicians is often based on the objective measure of bowel movement (BM) frequency, patients tend to include other manifestations, such as straining, feelings of incomplete evacuation, abdominal pain/bloating, and hard, lumpy, small stools.[2] In fact, infrequent defecation is one of the least-reported constipation symptoms. For instance, in an Internet-based survey of 4,680 patients with constipation, infrequent BMs were reported by only 57% of participants. Other constipation-associated symptoms were reported at higher frequencies: straining (79%), gas (74%), hard stool consistency (71%), and abdominal discomfort (62%).[3]

In the search for a universally agreed upon definition for constipation, international experts in functional GI disorders have developed formal criteria (e.g., Rome II criteria, **TABLE 1**) based on key symptomatic features of this disorder.[4,5] Although these symptom-based criteria may help standardize the enrollment of patients into clinical trials, some experts have deemed their use impractical in clinical practice.[5] In a recently published position statement on the management of chronic constipation, the American College of Gastroenterology (ACG) Task Force advocates a broader definition: "Constipation is a symptom-based disorder and is characterized by infrequent defecation, difficult stool passage, or both," with chronic constipation defined as the presence of these symptoms for at least three months (**TABLE 1**).[5]

Table 1

Definitions of Constipation

Rome II Diagnostic Criteria for Functional Constipation[4]	**American College of Gastroenterology Task Force Definition of Constipation**[5]
Fewer than three bowel movements per week with no evidence of organic disease and/or: • Hard or lumpy stools • Straining • Sensation of incomplete evacuation • Sensation of anorectal obstruction • Manual maneuvers needed to pass stool for >25% of defecations, for ⩾12 weeks of the last 12 months In addition to the above, the patient must not meet Rome II criteria for irritable bowel syndrome	Unsatisfactory defecation characterized by one or both of the following: • Infrequent stools • Difficult stool passage • Straining • Sense of difficulty passing stool • Incomplete evacuation • Hard/lumpy stools • Prolonged time to pass stool • Need for manual maneuvers to pass stool Constipation is considered "chronic" if these symptoms are present for ⩾3 months

Source: References 4, 5

Prevalence and Impact

Constipation affects 2% to 27% of the North American population,[6] or about eight million to 70 million people. The range of prevalence rates may be attributed to differences in definitions (e.g., self-report vs. Rome I or II criteria) and study design (e.g., phone interview vs. face to face); most estimates fall between 12% and 19%, with more than twice as many women as men affected.[6] Usually, constipation is an occasional inconvenience, but it can also be a chronic condition, lasting for several weeks or months to several years. For instance, in an epidemiologic survey conducted in 1997 (N = 10,018), 45% of female and 30% of male respondents who met symptom criteria for constipation in the three months preceding the survey (female, n = 1073; male, n = 403) reported symptoms lasting at least five years.[7] Symptoms associated with constipation negatively affect patients' social lives and their ability to perform activities of daily living.[8]

Given its prevalence, negative effect on patients' daily lives, and subsequent demand on health care resources, it is not surprising that constipation imposes a heavy economic impact in terms of direct costs (e.g., medical expenses in the inpatient and outpatient settings) and indirect costs (e.g., decreased productivity at school or work, work absenteeism). Cumulatively, it has been estimated that treating patients with constipation in the United States results in reimbursement costs of almost $19 million over a 15-month period.[8] Indirect costs associated with constipation are also substantial. The chronic nature of the condition can result in extended periods of bothersome symptoms that negatively affect patients' ability to attend or be productive at work or school. In a cross-sectional survey of 557 patients with chronic constipation (43% of whom were employed), 12% reported a 2.4-day mean absence from work or school during the previous month, and 60% reported impaired productivity while at work, amounting to a 21% mean decrease in productivity (equivalent to more than eight hours in a 40-hour workweek).[9] Furthermore, 72% of study participants reported impairment in their ability to perform daily activities.[9]

Causes

Awareness of the potential causes of constipation is critical to pharmacists' ability to properly triage patients with this disorder and to understand the clinical rationale for therapeutic treatment options. Constipation may be classified as primary or idiopathic (arising spontaneously or from an obscure or unknown cause) or as secondary (arising as a result of a specific condition or medication; **FIGURE 1**).[10,11] Many clinical conditions are recognized as potential secondary causes of

constipation; examples include endocrine, metabolic, and neurologic disorders and colon cancer. Medications are another common cause; common offenders are opiates, anticholinergics, and tricyclic antidepressants.[12,13]

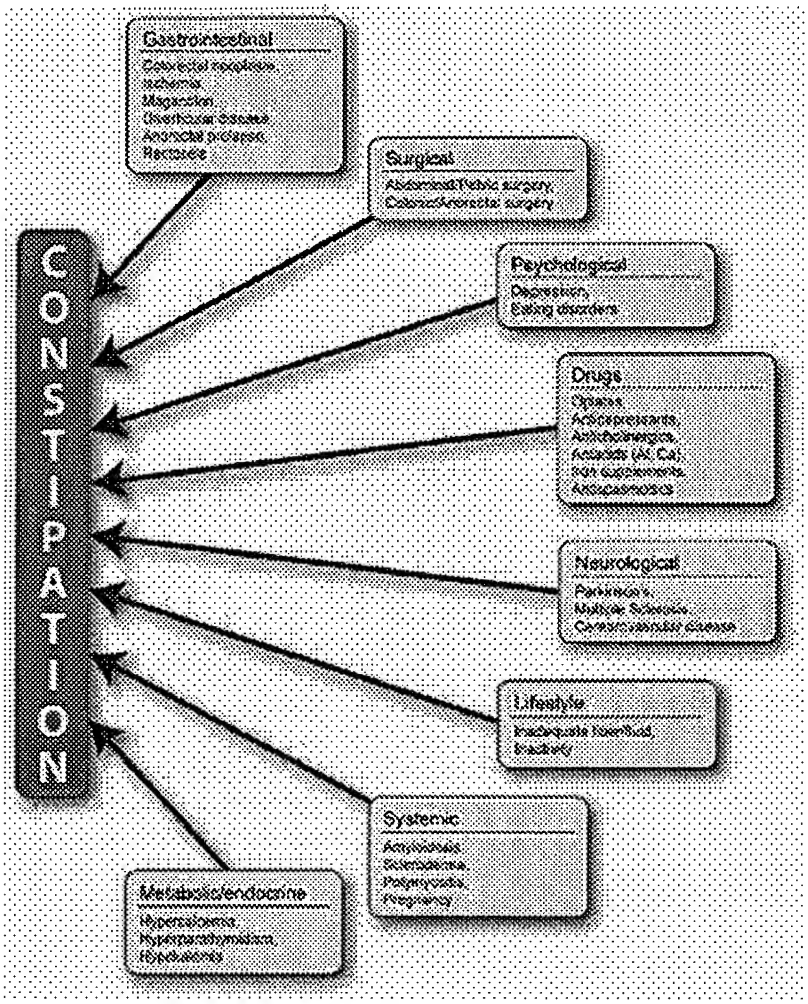


Figure 1. Select medication- and disease-related (secondary) causes of constipation[10,11]

Patients with primary constipation have no obvious underlying cause for their symptoms and are presumed to have a primary colonic motor dysfunction. Three broad categories of chronic constipation have been identified: normal transit, slow transit, and disorders of defecatory function. At any time, constipation-associated symptoms in a given patient may arise as a result of one or more of these mechanisms.[14] Normal-transit constipation is the most prevalent form, occurring in about 60% of patients with constipation of unknown cause.[14] As the name suggests, in patients with normal-transit constipation, stool progresses through the colon at a normal rate and bowel frequency is normal, yet patients feel constipated. They often have symptoms of bloating and abdominal pain/discomfort, the sensation of incomplete evacuation, and hard stools. These factors may result in reduced rectal compliance, reduced rectal sensation, or both.[14] Slow transit constipation is characterized by a prolonged delay in the transit of stool through the colon, possibly as a result of smooth muscle dysfunction or a disturbance in the enteric nervous system, which is the primary control center for gut motility. This condition particularly affects young women who experience one or fewer BMs weekly and is associated with bloating and abdominal pain/discomfort.[14] Defecatory disorder is a general term for a number of conditions characterized by a poorly functioning pelvic floor or anal sphincter. Select synonyms include *anismus*, *pelvic floor dyssynergia*, and *paradoxical pelvic floor contraction*.[14] These disorders can develop as a consequence of conscious, prolonged avoidance of defecation because of pain associated with the passage of large, hard stool or with an anal fissure or hemorrhoid. They can also develop as a result of structural abnormalities such as rectocele (inversion and prolapse of the rectum) or excessive peri-neal descent, although these anatomic causes are less commonly observed.

Ineffective rectal emptying can be caused by lack of coordination between the abdominal recto-anal and pelvic floor muscles during defecation.[14]

Triage in the Pharmacy: Key Factors to Consider and Questions to Ask

Given the numerous potential causes of constipation, responding to questions regarding self-treatment requires an organized approach aimed at determining the appropriateness of self-care versus referral for further evaluation. Below are key points pharmacists must consider in their interactions with patients (**TABLES 2 AND 3**).

Table 2

Important Questions to Ask Patients During Triage

Specific symptoms patient is experiencing

- What patient means by "constipation"
- Exact location of discomfort
- Severity of symptoms

Associated symptoms

- Abdominal discomfort/pain
- Bloating
- Straining

Medications tried to date

- Dose
- Duration
- Why patient discontinued medication

Table 3

Exclusions for Self-Treatment of Constipation

Presence of:

- Bloody/black or tarry stools
- Marked abdominal pain/discomfort
- Fever
- Nausea/vomiting
- Family history of inflammatory bowel disease or colon cancer
- Drastic change in severity or nature of symptoms
- Symptoms that have lasted longer than two weeks after self-treatment

- Ask the patient to *define what he or she means by constipation.* This is a critical first step because some patients may assume that their bowel patterns are abnormal. Pharmacists can help patients understand that there is no universally accepted definition of constipation and that the range of normal bowel frequency often spans from three BMs per day to three BMs per week.[15] Asking patients to describe the form of their stools (e.g., large, hard, lumpy) may also reveal important information. Because of the sensitive nature of the topic (and the potential lack of a private counseling area in the community pharmacy setting), the Bristol

Stool Scale (**FIGURE 2**) was devised as a simple clinical tool that can be used discreetly to help patients describe their stool patterns.[16] The visual depictions and associated descriptions on this scale correlate with potential pathophysiology. Patients should also explain their views of *treatment success* (e.g., goals regarding frequency and quality of BMs), because their expectations of therapy may be unrealistic (e.g., daily BM).

- Ask the patient to describe the associated symptoms he or she is experiencing (e.g., straining, abdominal pain/discomfort, bloating). As mentioned previously, for some patients, any of these associated aspects may represent the primary symptom (bothersomeness, negative effect on daily life), whereas BM frequency may not even be mentioned.
- As much as feasible, elicit *specific characteristics of the primary symptom*, including the exact location of the symptom—regardless of whether there is a temporal association of a symptom with an event—and factors that alleviate or aggravate the symptom.
- Have the patient describe the *treatments tried to date*, including dose and treatment duration, whether the treatments were effective, and why the treatments were discontinued. Answers may reveal potential reasons behind treatment failure, including inappropriate choice of drug for the symptoms treated and inadequate dose or treatment duration. The presence of a secondary cause of symptoms (**FIGURE 1**) may also explain treatment failure. It is critical to ask patients to list the medications, including OTC products, vita-min and mineral supplements, and herbal products, they are taking and to describe any comorbid conditions.
- Have the patient describe *symptom severity and duration* and assess for the *presence of alarm features (warning signs and symptoms)*. These are the principal factors determining the immediate need for referral. In general, symptom duration of less than three months refers to *occasional constipation*, a condition that typically responds to lifestyle changes and OTC treatments. Symptom duration of three months or longer, however, usually suggests *chronic constipation*, which should not be self-treated. This condition is often resistant to lifestyle changes and OTC treatments and necessitates a thorough physical examination, diagnostic evaluation, and prescription medication regimen.
- Regardless of symptom severity or duration, alarm features such as blood in the stool, dark/tarry stool, marked abdominal pain/distension/cramping, marked flatulence, fever, nausea, vomiting, or family history of colon cancer or inflammatory bowel disease, which are suggestive of organic disease, exclude self-care and require immediate referral for further evaluation. A sudden or drastic change in the severity or nature of symptoms or unexplained changes in bowel habits (particularly if accompanied by weight loss), as well as a recurrence of symptoms after dietary or lifestyle modifications or laxative use, are further exclusions for self-care. Finally, the presence of a potential secondary cause of constipation (e.g., paralysis) also prompts referral.[14]

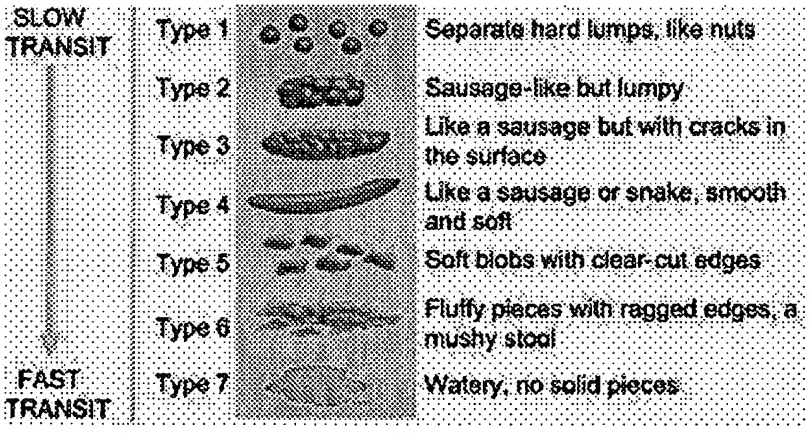


Figure 2. The Bristol Stool Scale[16]

Treatment Options

Dietary and Lifestyle Changes: Several nonpharmacologic treatments are generally recommended as the initial approach for managing constipation, including adequate hydration (1.5 to 2 L of fluid per day), increased consumption of dietary fiber, regular nonstrenuous physical exercise such as walking or swimming for at least 30 minutes per day, and dedicated bathroom

time. These lifestyle changes represent good overall health measures and can be tried by patients with occasional constipation before they initiate treatment with OTC products. The effectiveness of these treatments from an evidence-based perspective in patients with chronic constipation, however, has not been validated.[17,18]

Although inadequate fluid intake may result in decreased gastric distension and reduced peristalsis, studies have not uniformly shown a positive correlation between increased fluid ingestion and clinically relevant change in stool frequency.[19]

This approach may be most beneficial in patients who are dehydrated.[20] This generally harmless measure should be implemented with caution in patients (particularly the elderly) who have comorbid conditions, such as cardiovascular disease, that necessitate fluid restriction.[17]

A regular exercise routine is also generally beneficial. Physical activity has been shown to result in increased motility of the ascending and descending colon, both in patients with constipation and in the general population[20] and to be associated with an decreased prevalence of constipation in women.[21] Whether this observation reflects a direct causative relationship or whether other factors are involved (e.g., the underlying conditions that lead to constipation may decrease patients' ability to exercise) remains unclear. The general clinical opinion is that modest increases in physical activity may benefit patients with mild constipation, but evidence-based data demonstrating the effect of exercise on bowel function in those with more severe or chronic symptoms are lacking.[22]

Increased dietary fiber intake (to at least 25 g/day) is a cornerstone of constipation treatment, especially when combined with increased fluid intake. Fiber binds water in the GI tract and is believed to reduce colonic transit time and increase stool bulk and frequency.[20,23] Suggestions for increasing fiber intake include eating three to five daily servings of vegetables (e.g., cauliflower, string beans, broccoli, carrots), two to five fruits (e.g., apples, pears, oranges, peaches), and two to four servings of whole grain products (e.g., granola, bread, cereal, pasta).[11,24] Evidence-based support for these measures, however, is lacking. No proven relationship exists between decreased dietary fiber intake and presence of constipation, and the relationship between dietary fiber and colonic transit time remains unclear.[19] Also, pharmacists should keep in mind that although this approach may benefit some patients, those with severe constipation might experience a worsening of symptoms (e.g., increased gas and bloating) from greater consumption of fiber-rich foods.[24]

Laxatives: When lifestyle measures alone provide inadequate relief of constipation, a judicious trial with laxatives is usually the mainstay of treatment. Several classes of laxatives are available, including bulk-forming, emollient, osmotic, and stimulant. Although some laxatives are available only by prescription, most products are non-prescription, representing a substantial portion of the OTC section of pharmacy shelves. Patients are often overwhelmed at the large laxative selection and require the pharmacist's help. Laxatives differ in their mechanism of action, onset of effect, potential adverse effects, and precautions (**TABLE 4**).[14,24-26] Pharmacists need to be well versed in the similarities and differences among these agents and understand the patient populations for whom each category is best suited. The pharmacist must be equipped with this knowledge to counsel patients on realistic treatment expectations and guidelines for safe use. It is important to remember that laxatives are not intended for long-term (more than two weeks) use, and none are labeled for use by patients with chronic constipation.

Table 4

Select Characteristics of Commonly Used Laxatives

Laxative Type	Examples	Mechanism of Action	Onset of Effect	Potential Side Effects/Precautions
Bulk	Natural fiber Psyllium seed husk (e.g., Metamucil)	Increases the retention of water in the stool, leading to reduced stool consistency, increased stool volume, and	Psyllium and methylcellulose: 12–72 h	Gas, bloating, esophageal obstruction, colonic obstruction, calcium and iron malabsorption

		increased GI motility (decreased colonic transit time)		
	Semisynthetic fiber (e.g., Citrucel) Calcium polycarbophil (e.g., Fibercon)		Calcium polycarbophil: 24–48 h	
	Synthetic fiber (e.g., polycarbophil)			
Stool softener	Docusate (e.g., Colace) Docusate calcium (e.g., Surfak)	Acts primarily as surface-active agent, enhancing interaction of water with stool, resulting in softer stool		Efficacy in the treatment of constipation not well established
Osmotic	Saline Magnesium hydroxide (e.g., milk of magnesia) Magnesium citrate (e.g., Evac-Q-Mag, Citroma) Magnesium sulfate Sodium phosphate	Retains water in the intestinal lumen by creating an osmostic gradient	Saline: 30 min to 3 h	Electrolyte abnormalities (e.g., hypermagnesemia, hyperphosphatemia, hyponatremia, hypokalemia) can occur. Use with caution in patients with compromised renal orcardiac function
	Poorly absorbed sugars **Lactulose** (e.g., Kristalose) Sorbitol (Cytosol) Glycerine suppositories		Poorly absorbed sugars: 24–48 h	Hypovolemia, diarrhea, abdominal cramping, bloating, gas
	Polyethylene glycol (e.g., MiraLax)		**PEG**: 24–48 h	Bitter taste and diarrhea
Stimulant	Diphenylmethane derivative Bisacodyl (e.g., Dulcolax, Correctol)	Affects mucosal transport and motility by decreasing absorption of, and inducing secretion of, water and ions	Bisacodyl: 6–12 h	Electrolyte imbalances (e.g., hypokalemia), abdominal discomfort, gas potential for overuse/abuse
	Anthraquinones Senna (e.g., Senokot)		Senna: 6–12 h	Link with damage to colonic mucosa or the enteric nervous systempoorly established
Source: References 14, 24-26				

Optimal product selection ultimately depends on patient-specific factors, including the patient's symptoms, the goal of therapy, comorbid conditions, and possible side effects. Onset of effect is an important distinguishing factor among agents. For example, saline laxatives have a rapid onset of

action (0.5 to 3 hours), making them suitable for use in patients seeking rapid symptom relief.[25]

Bulk laxatives, on the other hand, exhibit a slow onset of action (12 to 72 hours), limiting their usefulness in patients seeking prompt BMs. However, patients who experience abdominal pain when using stimulant laxatives may prefer a bulk type despite the slower action. Possible adverse effects are also an important consideration in product selection. The poorly absorbed ions (**lactulose** and sorbitol), as well as some bulk laxatives (e.g., psyllium), are fermented by bacteria in the colon and may produce flatulence and distension. Osmotic (e.g., magnesium salts) and certain stimulant laxatives (e.g., senna) are associated with various electrolyte abnormalities and should be used with caution in patients with compromised cardiac or renal function.[14,26] Metabolically inert laxatives that are resistant to bacterial fermentation, such as calcium polycarbophil, methylcellulose, and polyethylene glycol (**PEG**), are less likely to cause GI-related adverse effects.[25] Although it has been suggested that the extended use of laxatives by patients with chronic constipation causes damage to the autonomic nervous system, such evidence has been based on observational investigations rather than well-controlled studies, and a causal relationship has not been documented.[20] Long-term use of laxatives has also been associated with an increased risk for colon cancer; however, it is unclear whether this association is a feature of the treatment or of the chronic nature of the condition.[20] In general, patients should be encouraged to avoid excessive use of laxatives and warned that even after excessive use is discontinued, it may take four to six weeks for bowel function to normalize.[24]

High-quality, evidence-based data evaluating laxatives in the treatment of patients with chronic constipation are lacking. Findings from two recently published systematic reviews of clinical trials of therapies for chronic constipation are helpful in gauging the general role of laxatives in therapy.[5,18] Based on the parameters set forth by Ramkumar and Rao (**TABLE 5**), **PEG** was the only laxative shown in key clinical trials to improve BM frequency, stool consistency, and colonic transit time, thus leading to a grade A rating.[18] All formulations of **PEG**, including PMF-100, **PEG** 3350, **PEG**/electrolyte solutions, and high-molecular weight **PEG** (**PEG** 4000), were included in this analysis. Of these agents, only **PEG** 3350 (MiraLax) is approved by the FDA for use in patients with constipation, specifically in those with occasional constipation. Psyllium and **lactulose** both received a grade B rating for their usefulness in improving stool frequency and consistency, and the remaining laxatives studied (magnesium hydroxide, calcium polycarbophil, methylcellulose, senna, bisacodyl, docusate, and bran) received a grade C rating.

Table 5

Parameters Used in Systematic Reviews of Agents Used to Treat Patients with Chronic Constipation: Ramkumar and Rao

Grade	Evidence	Examples
A	Level 1: Consistent results from well-designed, well-conducted studies (good quality)	Polyethylene glycol (**PEG**)
B	Level 2: Results show benefit, but strength is limited by the number, quality, or consistency of the individual studies (fair quality)	Psyllium **Lactulose**
C	Level 3: Insufficient because of limited number or power of studies or flaws in design or conduct (poor quality)	Magnesium hydroxide Calcium polycarbophil Methylcellulose Senna Bisacodyl Docusate Bran

Source: Reference 18

In a systematic review of the treatment of patients with chronic constipation, the ACG Task Force established preset parameters for its recommendations (**TABLE 6**).[5] Based on these parameters, psyllium, calcium polycarbophil, methylcellulose, bran, stool softeners, milk of magnesia, and

stimulant laxatives received a grade B recommendation; in most cases, the task force concluded that the data were insufficient to make a recommendation about the efficacy of these agents in patients with chronic constipation. **Lactulose** and **PEG** both received a grade A recommendation for their efficacy in improving stool frequency and stool consistency. However, data on adverse effects were not adequately reported. Use of **lactulose** was associated with abdominal pain, and high doses of **PEG** resulted in an incidence of diarrhea ranging from 2% to 40%. Furthermore, as in the systematic review by Ramkumar and Rao,[18] it must be noted that all formulations of **PEG**, as well as a trial in patients with opioid-induced constipation, were included in this analysis. The two trials involving **PEG** 3350 received quality scores of 3, which is not consistent with a well-designed, randomized, controlled trial; both were of short duration (two weeks), and one was a crossover design with few patients (N = 23). The results of these two systematic reviews highlight the dearth of high-quality clinical data to support the use of many commonly used therapies for chronic constipation.

Table 6

Parameters Used in Systematic Reviews of Agents Used to Treat Patients with Chronic Constipation: ACG Task Force

Grade	Support	Evidence	Examples
A	Two or more level 1 trials without conflicting evidence from other level 1 trials	Level 1: RCTs with $P<.05$; adequate sample size; appropriate methodology (high quality)	**PEG** **Lactulose** Tegaserod
B	Single level 1 trial *or* 2 or more level 1 trials with conflicting evidence from other level 1 trials *or* 2 or more level 2 trials	Level 2: RCTs with $P<.05$; or inadequate sample size; and/or appropriate methodology (intermediate quality)	Psyllium Calcium polycarbophil Methylcellulose Bran Stool softeners Milk of magnesia Stimulant laxatives
C	Level 3 to 5 trials	Level 3: Non-RCTs with contemporaneous controls Level 4: Non-RCTs with historical controls Level 5: Case series	Herbal supplements Alternative treatments Lubricants Combination laxatives

Source: Reference 5

Constipation in Pregnancy

Constipation is reported in 11% to 38% of pregnant women, occurring most often as a result of increased levels of circulating progesterone.[27] Iron-containing supplements are also a common cause of constipation during pregnancy. Because of the limited evidence of the safety of using laxatives during pregnancy, the first treatment approach should be dietary measures, including increased fluid intake and fiber supplements. Other treatment options that appear to be safe during pregnancy include the prophylactic use of docusate or the use of senna, bisacodyl, or **lactulose**. Because of the associated side effects, mineral oil (which can decrease vitamin absorption), castor oil (which can cause premature labor), and saline laxatives (which can lead to electrolyte imbalances) should be avoided during pregnancy.[28,29]

A Cochrane review for constipation treatments during pregnancy confirmed the lack of good-quality evidence in this setting.[27] Only two suitable trials were identified for the review. Results of one trial revealed that fiber supplements increased the frequency of defecation (odds ratio, 0.18; 95% CI, 0.05 to 0.67) and led to softer stools. Results of the second trial showed that stimulant laxatives were more effective than bulk-forming laxatives (odds ratio, 0.30; 95% CI, 0.14 to 0.61). The reviewers concluded that dietary supplements of bran or wheat fiber are likely to help relieve constipation during pregnancy and appear to have no adverse effects. However, if constipation persists, stimulant laxatives are likely to be more effective but may cause more side effects (e.g., diarrhea, abdominal pain).

General Recommendations

In general, for patients with occasional constipation who have not previously self-treated their condition (and in whom self-treatment is appropriate), an increase of dietary fiber (to 20 to 40 g/day) or using a bulk-forming laxative is a reasonable first step. Although the efficacy of bulk laxatives has not been shown to be superior to that of other laxatives, bulk laxatives are generally considered safe. Osmotic laxatives (e.g., magnesium salts, **lactulose**, **PEG**) are usually tried next, and stimulant laxatives are reserved for patients in whom other agents have failed. The usefulness of the stool softener docusate in the outpatient setting (particularly for patients with chronic constipation) is generally considered limited based on the lack of demonstrated efficacy in controlled trials.[22,24]

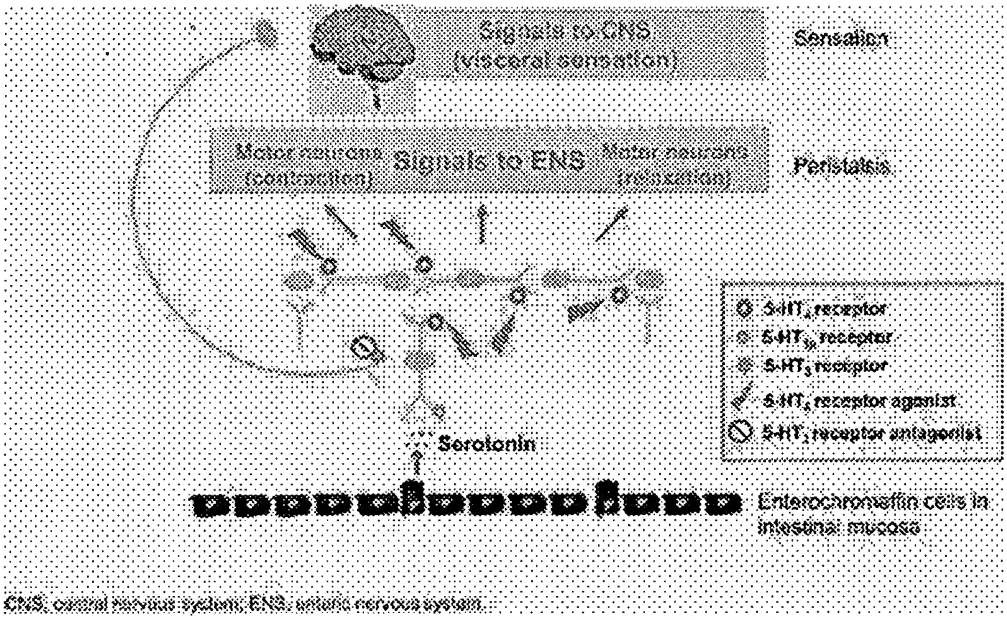
New Directions in Constipation Treatment

Patients are often dissatisfied with the efficacy or adverse effects of traditional constipation treatments.[18] In the Internet-based survey of 4,680 patients with constipation, only 53% of respondents were completely satisfied with their treatment regimens.[3] Lack of medication efficacy was the most commonly cited reason for dissatisfaction. More than two thirds (68%) of respondents stated that they were not completely satisfied with the efficacy of OTC laxatives in improving their quality of life.

Sample case scenario #1

Angela D. is a 35-year-old, generally healthy, stay-at-home mother with a three-week history of constipation that has not responded to dietary fiber. She does not have comorbid conditions and is not experiencing any warning signs or symptoms that exclude self-care. She asks the pharmacist for help in selecting an OTC laxative. The pharmacist advises her to maintain a regular exercise routine, continue to include fiber in her diet, and drink an adequate amount of fluid (eight glasses of water) every day. If these measures provide inadequate relief, he recommends trying an osmotic laxative, such as magnesium hydroxide. He also informs Angela that with this agent she can expect to have a bowel movement within 30 minutes to three hours but that potential adverse effects include abdominal cramping, gas, or bloating.

Serotonergic Receptor Agonists for Chronic Constipation: Neurotransmitter alterations have been identified as one of numerous potential underlying abnormalities associated with constipation.[30] Serotonin (also known as 5-hydroxytryptamine [5-HT]) is a prominent neurotransmitter in the gut. Acting in conjunction with other signaling molecules, it has a key role in the initiation and maintenance of peristalsis, the enhancement of intestinal secretion, and the modulation of pain sensation in the bowel (**FIGURE 3**).[31] Recent research advances have demonstrated an association between chronic constipation and alterations in serotonin synthesis and signaling.[30] Of the 14 serotonin receptor subtypes identified to date, type 3 (5-HT_3) and type 4 (5-HT_4) are among the most relevant to GI tract function and perception of pain.[31] The activation of 5-HT_3 receptors enhances motility, secretion, and sensation; 5-HT_3 receptor antagonists, such as alosetron (Lotronex), thus slow colonic transit, increase fluid absorption, and attenuate visceral nociception.[31] Activation of 5-HT_4 receptors can directly excite or inhibit neural and smooth muscle cells (depending on their specific location within the GI tract). 5-HT_4 receptor agonists such as tegaserod (Zelnorm) have a major role in enhancing the peristaltic reflex[31] and have also been shown to modulate stool fluid content[32] and reduce visceral sensation.[30]



Adapted with permission from: Grider et al. Gastroenterology. *1998;115:370; Gershon.* J Clin Gastroenterol. *2005;39(4 suppl 3):S184; and Baker.* Am J Health Syst Pharm. *2005;62(7):705.*

Figure 3. Role of Serotonin in GI Tract Function

The usefulness of 5-HT_4 receptor agonists in accelerating intestinal transit in patients with constipation has been demonstrated with several agents, including the benzamide derivatives cisapride (Propulsid) and prucalo-pride;[33,34] however, neither agent is readily available (cisapride can be accessed via special programs, whereas studies with prucalopride have been suspended) because of serious cardiac-related safety concerns thought to be related to their specific chemical structure (benzamide, benzofuran) rather than 5-HT_4 receptor agonist activity.[33]

Tegaserod is a selective 5-HT_4 receptor agonist that is the first in a new chemical class called aminoguanidine indoles. It has been shown to augment the peristaltic reflex, increase intestinal secretion, and decrease GI visceral hyper-sensitivity.[31] Tegaserod was approved by the FDA in July 2002 for the treatment of women with irritable bowel syndrome whose primary bowel symptom is constipation, and in August 2004, it became the first agent approved for the treatment of patients (men and women younger than 65 years) with chronic idiopathic constipation.[35] Approval for this additional indication was based on data from two well-designed, randomized, placebo-controlled trials in which tegaserod significantly increased BM frequency and provided relief of the multiple symptoms of chronic constipation, including straining, hard stools, incomplete evacuation, infrequent defecation, bloating, and abdominal discomfort.[36,37] In these trials, the onset of effect was short; patients experienced their first spontaneous BMs (achieved without the use of laxatives, enemas, or digital manipulation) within a median of 18 hours.[36,37] Tegaserod was generally well tolerated in these trials. Diarrhea was the most frequently reported adverse event, occurring in 6.6% of patients receiving tegaserod 6 mg twice daily compared with 3% in those receiving placebo.[35] However, most episodes were mild to moderate in severity, occurred early during treatment, and resolved quickly without the need for antidiarrheal treatment.[36,37] Additionally, tegaserod use has not been associated with cardiac abnormalities.[38]

In the systematic review by Ramkumar and Rao, tegaserod received a grade A rating based on the quality of the clinical trials.[18] Congruently, the ACG Task Force found tegaserod to be effective at increasing the occur-rence of complete spontaneous BMs, relieving straining, and improving stool frequency and stool consistency in patients with chronic constipation. The ACG Task Force also gave it a grade A recommendation.

The association between the use of select serotonergic agents and the development of ischemic colitis (a vascular condition caused by reduced blood flow to the colon) has raised substantial concern among the medical community.[39] There was no report of patients with this condition in tegaserod clinical trials. Although some incidences of transient ischemic colitis (with no serious

long-term consequences) were reported during postmarketing surveillance, their rate was consistent with the rate expected in the general population and lower than that observed in patients with IBS.[40] To date, no vascular mechanism has been identified that could lead to mesenteric or colonic ischemia with the use of tegaserod.[41] Regardless, the prescribing information for tegaserod lists ischemic colitis as a precaution and directs immediate discontinuation if patients develop symptoms—including "rectal bleeding, bloody diarrhea, or new or worsening abdominal pain"—consistent with it.[35]

Sample case scenario #2

Barbara, a 52-year-old teacher, seeks treatment for a six-month history of constipation. After using the Bristol Stool Scale as a guide, she reports having large, hard stools that require her to strain with most bowel movements. During the past five months, she has tried several OTC products without success. Her symptoms continue to cause discomfort and are starting to negatively affect her ability to work productively. After establishing the chronic nature of her symptoms and the previous medications that she has tried, the pharmacist refers her to her primary care provider for a complete medical evaluation. One week later, the patient returns to the pharmacy with a prescription for tegaserod for chronic constipation.

When dispensing the prescription, the pharmacist explains to Barbara that tegaserod 6 mg should be taken twice daily. She can expect to experience improvement in the frequency of movements and in stool consistency and straining. The first bowel movement is typically achieved within the first 18 hours of treatment. Diarrhea has been reported with this agent, but it is generally mild, transient, and resolves with continued treatment. If, however, she experiences severe diarrhea that does not go away on its own or a new onset of abdominal pain or rectal bleeding, she should discontinue treatment and contact her physician immediately.

Emerging Treatments for Chronic Constipation

Several additional drug classes, including opioid receptor antagonists, chloride channel activators, neurotrophin-3, and sodium phosphate, are under investigation for the treatment of patients with constipation.

- *Opioid receptor antagonists.* Endogenously, opiates act through the delta-opiate receptor to slow peristalsis in the gut. As a result, exogenous opiate use for analgesia is frequently associated with constipation. Antagonists of the delta-opiate receptor thus have the potential to relieve constipation in many patients who experience adverse effects while taking opioids.[33] This approach is complicated by the fact that most current opioid antagonists are able to cross the blood-brain barrier, thereby reducing both the analgesiaand the constipation-induced effects of opioid agonist therapy. Recent clinical trials with two peripheral opioid antagonists, alvimopan and methylnaltrexone, suggest that these agents may be useful in reducing opiate-induced constipation and postoperative ileus.[33] Whether the peripheral effects of these agents will effectively relieve the centrally induced constipation associated with delta-opiate agonists remains to be established.[33] Alvimopan and methylnaltrexone may also enhance intestinal secretion by blocking endogenous opioid-induced inhibition of fluid and electrolyte secretion from the GI tract.[33]
- *Chloride channel activators.* Fluid secretion in the gut is dependent on chloride transport.[33] Lubiprostone is a bicyclic fatty acid that has been shown to facilitate chloride secretion through the activation of a chloride-mediated inward current.[42] In placebo-controlled clinical trials, patients receiving lubiprostone experienced significant increase in the frequency of spontaneous BMs compared with those receiving placebo, with most patients experiencing a BM within 24 hours of their first dose. Patients receiving lubiprostone also experienced significant improvements in straining and stool consistency scores compared with those receiving placebo.[43] The most common adverse events associated with treatment were nausea, diarrhea, and headache; frequency percentages were not reported.

- *Neurotrophin-3.* Exogenous neurotrophic factors (substances that can stimulate the growth and maintenance of cells) have been shown to stimulate gut motility. In clinical trials with neutrophin-3 for the treatment of patients with Parkinson's and Alzheimer's diseases, it was noted that diarrhea was a prominent adverse effect associated with therapy.[33] Results of a double-blind, four-week study in 107 patients with functional constipation confirm this observation.[44] In this study, neurotrophin-3 (9 mg) administered three times weekly significantly increased BM frequency, improved stool passage, and softened stool consistency, compared with placebo. Adverse effects in patients receiving neutrophin-3 included injection-site reactions (n = 6), upper respiratory tract infections (n = 3), and flatulence, nausea, flushing, and paresthesias (n = 2 each). These studies demonstrate the therapeutic potential of neurotrophin-3 for the treatment of constipation; however, longer-term studies are required to assess the safety of this agent. In this study, 50% of patients developed antibodies to neurotrophin-3; the long-term consequences of this finding are unknown.
- *Sodium phosphate.* Sodium phosphate has traditionally been used to aid bowel cleansing before colonoscopy. Preliminary studies in healthy volunteers suggest that it also can increase the frequency of BMs and can help improve stool consistency.[45] In a four-week open-label study, patients with chronic constipation received four or eight sodium phosphate tablets (1.5 g sodium phosphate per tablet). The dose could subsequently be increased or decreased for 28 days, according to each patient's bowel habits. At the end of treatment, 100% of patients who initiated treatment on four tablets per day and 95.8% of those who initiated treatment on eight tablets per day experienced an increase of at least one BM per week above baseline assessment. Nausea (n = 5), diarrhea (n = 4), and bloating (n = 2) were the most frequently reported adverse events considered possibly or definitely related to treatment, but no patient reported a serious adverse event. Further data are required to assess the suitability of sodium phosphate tablets in the long-term management of chronic constipation.

Conclusion

Constipation is a highly prevalent, often bothersome disorder that negatively affects patients' social and professional lives and results in frequent use of the health care system. Pharmacists can have a vital role in helping patients manage constipation in a safe and effective manner. By understanding the key questions to ask (during initial and follow-up patient encounters) and the signs and symptoms that suggest the need for further evaluation, pharmacists can work in collaboration with other health care providers to optimize patient care.

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Treating Chronic Constipation
Source: *Geri On The Spot*
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Constipation is one of the most common complaints in older adults, but physicians have a growing number of treatment options. Some are as familiar as over-the-counter laxatives or dietary changes; others are newly approved pharmaceutical products that have only recently moved into the supply chain.

"Patients develop tolerance to any and all therapies we have available," said Lin Chang, MD, David Geffen School of Medicine, University of California Los Angeles. "Few treatments will deal with all of a patient's symptoms, so you can expect to use combination therapies."

Many patients with constipation self-treat, she told a Saturday breakfast symposium sponsored by Sucampo Pharmaceutical and Takeda Pharmaceuticals North America. Supermarket and drug store shelves are filled with fiber supplements, bulking agents, osmotics, stimulant/irritant laxatives, lubricants, stool softeners, and other OTC agents.

All of these agents help some patients some of the time, but none help all patients, she noted. Other common approaches to treating constipation include better hydration, exercise, dietary changes to boost fiber consumption, and a dedicated time to have a bowel movement.

Defining Constipation

One aspect of variable effect is the variable definition of constipation. Among community-dwelling elderly patients, 30% report constipation at least monthly, said Eric Tangalos, MD, Mayo Clinic College of Medicine. In the nursing home population, the incidence of constipation rises to 70%. But there are several competing definitions of constipation that overlap in some areas

Dr. Tangalos suggested following the Rome II criteria, published in 1999. Criteria include infrequent stools, hard or lumpy stools, excessive straining during defecation, sensation of anal blockage, incomplete evacuation, and self-digitation.

Constipation requires two or more of these symptoms for at least 25% of the time for at least six months. "There is very little evidence that age alone is the culprit," Dr. Tangalos said. "The culprit is all of the factors that go with age."

Primary risk factors for chronic constipation include female gender, increasing age, medication use (antihypertensive, antidepressants, anti-Parkinsonism drugs, opiates, antihistamines, nonsteroidal anti-inflammatories, antacids, and others), anatomic problems, poor fiber intake, poor intake of solid food, and dehydration.

Pharmacotherapies

The US Food and Drug Administration has approved four agents for constipation, Dr. Chang said. Two osmotics, **lactulose** and polyethylene glycol (**PEG**), are indicated for occasional or short-term use. **Lactulose** can induce gas and bloating and is not tolerated by many patients, she added. **PEG** is commonly used off-label for chronic constipation, Dr. Chang added, although clinical trial data extends only to two weeks.

Two agents have been approved for chronic constipation, tegaserod and lubiprostone. Tegaserod is a 5-HT_4 receptor agonist that mimics serotonin and stimulates the peristaltic reflex, which accelerates transit.

Lubiprostone is a chloride channel activator that was approved by FDA in January, 2006. It acts by increasing fluid content secreted into the small intestine, which increases the net fluid content delivered to the colon and helps accelerate transport speed.

All of these agents show similar efficacy after three weeks of use. Patients taking **PEG** reported slightly over four spontaneous bowel movements weekly. Patients taking tegaserod reported just over five spontaneous bowel movements. Patients taking lubiprostone reported 7.5 spontaneous bowel movements the first week, falling to 6.5 in week two and just over 5 in the third week.

Two new agents are still in clinical trials, Dr. Chang said. Alvimopan is a peripherally acting mu-opioid antagonist that acts against opiate-induced constipation. It is not centrally active and has no effect on analgesia. Renzapride, a combined 5-HT_4 agonist/5-HT_3 antagonist appears to help bowel symptoms and colonic transit in irritable bowel syndrome with constipation.